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 ********** STN Columbus **********
FILE 'HOME' ENTERED AT 13:04:06 ON 09 JUL 2001
=> file biosis caba caplus embase lifesci medline scisearch uspatfull japio
=> e gicquel brigitte/au
E1        1    GICQUEL BRIGETTE/AU
E2        1    GICQUEL BRIGITE/AU
E3      151 --> GICQUEL BRIGITTE/AU
E4        2    GICQUEL BRIGITTE M E/AU
E5        1    GICQUEL BRITTE/AU
E6      136    GICQUEL C/AU
E7        6    GICQUEL CATHERINE/AU
E8       27    GICQUEL CHRISTINE/AU
E9        3    GICQUEL D/AU
E10       2    GICQUEL DANIEL/AU
E11      10    GICQUEL E/AU
E12       1    GICQUEL E J/AU
=> s e1-e4 and tuberculosis
L1      104 ("GICQUEL BRIGETTE"/AU OR "GICQUEL BRIGITE"/AU OR "GICQUEL BRIGI
          TTE"/AU OR "GICQUEL BRIGITTE M E"/AU) AND TUBERCULOSIS
=> dup rem l1
PROCESSING COMPLETED FOR L1
L2       73 DUP REM L1 (31 DUPLICATES REMOVED)
=> d bib ab 1-
YOU HAVE REQUESTED DATA FROM 73 ANSWERS - CONTINUE? Y/(N):y

L2  ANSWER 1 OF 73  CAPLUS  COPYRIGHT 2001 ACS
AN  2001:31632  CAPLUS
DN  134:111206
TI  Method of making and identifying attenuated microorganisms, compositions
    utilizing the sequences responsible for attenuation, and preparations
    containing attenuated microorganisms
IN  ***Gicquel, Brigitte*** ; Guilhot, Christophe; Camacho, Luis
PA  Institut Pasteur, Fr.
SO  PCT Int. Appl., 159 pp.
    CODEN: PIXXD2
DT  Patent
LA  English
FAN.CNT 1
    PATENT NO.      KIND  DATE      APPLICATION NO.  DATE
    --------------- ----  --------  --------------- --------
PI  WO 2001002555   A1    20010111  WO 2000-IB950   20000706
      W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
         CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR,
         HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT,
         LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU,
         SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN,
         YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
      RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
         DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ,
         CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
PRAI US 1999-142982   P  19990706
    US 1999-142833    P  19990708
AB  A functional genomic approach for identification of mutants of
    microorganisms that are unable to grow under certain specific conditions
    is disclosed. In one aspect of the invention, a method is provided in
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which a library of signature tagged transposon mutants (STM) is constructed and screened for mutants attenuated in pathogenicity. The method is esp. useful for identifying loci involved in pathogenicity. The method is well suited to identification of mutant actinomycetales, such as mycobacteria. To perform an STM in M. ***tuberculosis*** , plasmid pCG113 was constructed, comprising a temp.-sensitive-sacB vector carrying an IS1096 deriv. with a unique restriction site permitting the insertion of DNA signature tags. This allows efficient counter-selection of the plasmid at 39.degree. on sucrose and isolation of large nos. of M. ***tuberculosis*** transposition mutants. The method is useful for, among other things, drug discovery and construction of vaccines.

RE.CNT 14

RE

(1) Connaught Lab; WO 9910475 A 1999 CAPLUS

(2) Cornell Res Foundation Inc; WO 9850402 A 1998 CAPLUS

(3) Coulter, S; MOLECULAR MICROBIOLOGY 1998, V30(2), P393 CAPLUS

(4) Guilhot, C; JOURNAL OF BACTERIOLOGY 1994, V176(2), P535 CAPLUS

(5) Hensel, M; SCIENCE 1995, V269, P400 CAPLUS

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 2 OF 73 USPATFULL

AN 2001:93348 USPATFULL

TI Mycobacteria functional screening and/or expression vectors

IN ***Gicquel, Brigitte*** , Paris, France
Lim, Eng Mong, Paris, France
Portnoi, Denis, Paris, France
Berthet, Francois-Xavier, Paris, France
Timm, Juliano, Paris, France

PA Institut Pasteur, Paris Cedex, France (non-U.S. corporation)

PI US 6248581 B1 20010619
WO 9607745 19960314

AI US 1997-793701 19970609 (8)
WO 1995-FR1133 19950830
19970609 PCT 371 date
19970609 PCT 102(e) date

PRAI FR 1994-104585 19940902

DT Utility

EXNAM Primary Examiner: Swartz, Rodney P.

LREP Finnegan, Henderson, Farabow, Garrett & Dunner, L.L.P.

CLMN Number of Claims: 21

ECL Exemplary Claim: 1

DRWN 19 Drawing Figure(s); 18 Drawing Page(s)

LN.CNT 1360

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Recombinant screening, cloning and/or expression vector characterized in that it replicates in mycobacteria and contains 1) a mycobacteria functional replicon; 2) a selection marker, 3) a reporter cassette comprising a) a multiple cloning site (polylinker) b) a transcription terminator which is active in mycobacteria and is located upstream of the polylinker, and c) a coding nucleotide sequence derived from a gene coding for an expression, export and/or secretion protein marker, the nucleotide sequence being deprived of its initiation codon and its regulating sequences. This vector is used for identification and expression of exporter polypeptides, such as the Mycobacterium ***tuberculosis*** P28 antigen.

L2 ANSWER 3 OF 73 USPATFULL
AN 2001:75171 USPATFULL
TI Recombinant immunogenic actinomycetale
IN ***Gicquel, Brigitte*** , Paris, France
Winter, Nathalie, Paris, France
Gheorghiu, Marina, Neuilly-sur-Seine, France
PA Institut Pasteur, Paris, France (non-U.S. corporation)
PI US 6235518 B1 20010522
WO 9325678 19931223
AI US 1994-157152 19940726 (8)
WO 1992-EP1343 19920612
19940726 PCT 371 date
19940726 PCT 102(e) date
PRAI GB 1991-401601 19910614
DT Utility
EXNAM Primary Examiner: Minnifield, Nita
LREP Oblon, Spivak, McClelland, Maier & Neustadt, P.C.
CLMN Number of Claims: 31
ECL Exemplary Claim: 1
DRWN 9 Drawing Figure(s); 6 Drawing Page(s)
LN.CNT 834
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A mycobacteria transformed with an antigen-encoding gene, such as nef, under the control of a Streptomyces stress-responsive promoter, such as the S. albus groES/groEL1 promoter, and preferably associated with a synthetic ribosome binding site. The recombinant mycobacteria can be used as a vaccine against, for example, a pathogen which carries the antigen.

L2 ANSWER 4 OF 73 USPATFULL
AN 2001:40253 USPATFULL
TI Desaturase antigen of Mycobacterium ***tuberculosis***
IN Jackson, Mary, Paris, France
Gicquel, Brigitte , Paris, France
PA Institut Pasteur, France (non-U.S. corporation)
PI US 6204038 B1 20010320
AI US 1999-422662 19991022 (9)
RLI Division of Ser. No. US 1997-917299, filed on 25 Jul 1997, now patented, Pat. No. US 6010855
PRAI US 1996-22713 19960726 (60)
DT Utility
EXNAM Primary Examiner: Nashed, Nashaat T.
LREP Finnegan, Henderson, Farabow, Garrett & Dunner, L.L.P.
CLMN Number of Claims: 3
ECL Exemplary Claim: 1
DRWN 12 Drawing Figure(s); 12 Drawing Page(s)
LN.CNT 650
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to the isolation of a new gene, des, which encodes a M. ***tuberculosis*** protein named DES. The des gene appears to be conserved among different Mycobacteria species. The amino acid sequence of the DES protein contains two sets of motifs that are characteristic of the active sites of enzymes from the class II diiron-oxo protein family. Among this family of proteins, DES shares

significant homology with soluble stearoyl-ACP desaturases. DES is a highly antigenic protein, which is recognized by human sera from patients infected with M. ***tuberculosis*** and M. leprae but not by sera from tuberculous cattle. Thus, the DES protein provides a useful tool for the serodiagnostic analysis of ***tuberculosis*** .

L2 ANSWER 5 OF 73 CAPLUS COPYRIGHT 2001 ACS
AN 2001:436384 CAPLUS
TI Analysis of the phthiocerol dimycocerosate locus of Mycobacterium ***tuberculosis*** : evidence that this lipid is involved in the cell wall permeability barrier
AU Camacho, Luis R.; Constant, Patricia; Raynaud, Catherine; Laneelle, Marie-Antoinette; Triccas, James A.; ***Gicquel, Brigitte*** ; Daffe, Mamadou; Guilhot, Christophe
CS Unite de Genetique Mycobacterienne, Institut Pasteur, Paris, 75725, Fr.
SO J. Biol. Chem. (2001), 276(23), 19845-19854
CODEN: JBCHA3; ISSN: 0021-9258
PB American Society for Biochemistry and Molecular Biology
DT Journal
LA English
AB Among the few characterized genes that have products involved in the pathogenicity of Mycobacterium ***tuberculosis*** , the etiol. agent of ***tuberculosis*** , are those of the phthiocerol dimycocerosate (DIM) locus. Genes involved in biosynthesis of these compds. are grouped on a 50-kilobase fragment of the chromosome contg. 13 genes. Anal. of mRNA produced from this 50-kilobase fragment in the wild type strain showed that this region is subdivided into three transcriptional units. Biochem. characterization of five mutants with transposon insertions in this region demonstrated that (i) the complete DIM mols. are synthesized in the cytoplasm of M. ***tuberculosis*** before being translocated into the cell wall; (ii) the genes fadD26 and fadD28 are directly involved in their biosynthesis; and (iii) both the drrC and mmpL7 genes are necessary for the proper localization of DIMs. Insertional mutants unable to synthesize or translocate DIMs exhibit higher cell wall permeability and are more sensitive to detergent than the wild type strain, indicating for the first time that, in addn. to being important virulence factors, extractable lipids of M. ***tuberculosis*** play a role in the cell envelope architecture and permeability. This function may represent one of the mol. mechanisms by which DIMs are involved in the virulence of M. ***tuberculosis*** .
RE.CNT 35
RE
(2) Azad, A; J Biol Chem 1997, V272, P16741 CAPLUS
(3) Azad, A; Proc Natl Acad Sci U S A 1996, V93, P4787 CAPLUS
(4) Berthet, F; Sciences 1998, V282, P759 CAPLUS
(5) Brennan, P; Annu Rev Biochem 1995, V64, P29 CAPLUS
(6) Camacho, L; Mol Microbiol 1999, V34, P257 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 6 OF 73 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 1
AN 2001:180396 BIOSIS
DN PREV200100180396
TI Genomic sequence and transcriptional analysis of a 23-kilobase mycobacterial linear plasmid: Evidence for horizontal transfer and identification of plasmid maintenance systems.

AU Le Dantec, Corinne; Winter, Nathalie; ***Gicquel, Brigitte*** ; Vincent, Veronique; Picardeau, Mathieu (1)

CS (1) Unite de Bacteriologie Moleculaire et Medicale, Institut Pasteur, 28 Rue du Dr Roux, 75724, Paris Cedex 15: mpicard@pasteur.fr France

SO Journal of Bacteriology, (April, 2001) Vol. 183, No. 7, pp. 2157-2164. print.
ISSN: 0021-9193.

DT Article

LA English

SL English

AB Linear plasmids were unknown in mycobacteria until recently. Here, we report the complete nucleotide sequence of 23-kb linear plasmid pCLP from Mycobacterium celatum, an opportunistic pathogen. The sequence of pCLP revealed at least 19 putative open reading frames (ORFs). Expression of pCLP genes in exponential-phase cultures was determined by reverse transcriptase PCR (RT-PCR). Twelve ORFs were expressed, whereas no transcription of the 7 other ORFs of pCLP was detected. Five of the 12 transcribed ORFs detected by RT-PCR are of unknown function. Sequence analysis revealed similar loci in both M. celatum pCLP and the Mycobacterium ***tuberculosis*** chromosome, including transposase-related sequences. This result suggests horizontal transfer between these two organisms. pCLP also contains ORFs that are similar to genes of bacterial circular plasmids involved in partition (par operon) and postsegregational (pem operon) mechanisms. Functional analysis of these ORFs suggests that they probably carry out similar maintenance roles in pCLP.

L2 ANSWER 7 OF 73 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 2

AN 2001:176780 BIOSIS

DN PREV200100176780

TI High-resolution minisatellite-based typing as a portable approach to global analysis of Mycobacterium ***tuberculosis*** molecular epidemiology.

AU Mazars, Edith; Lesjean, Sarah; Banuls, Anne-Laure; Gilbert, Michele; Vincent, Veronique; ***Gicquel, Brigitte*** ; Tibayrenc, Michel; Locht, Camille; Supply, Philip (1)

CS (1) Laboratoire des Mecanismes Moleculaires de la Pathogenese Bacterienne, Institut National de la Sante et de la Recherche Medicale, U447, Institut Pasteur de Lille, 1, Rue du Prof. Calmette, F-59019, Lille Cedex: philip.supply@pasteur-lille.fr France

SO Proceedings of the National Academy of Sciences of the United States of America, (February 13, 2001) Vol. 98, No. 4, pp. 1901-1906. print.
ISSN: 0027-8424.

DT Article

LA English

SL English

AB The worldwide threat of ***tuberculosis*** to human health emphasizes the need to develop novel approaches to a global epidemiological surveillance. The current standard for Mycobacterium ***tuberculosis*** typing based on IS6110 restriction fragment length polymorphism (RFLP) suffers from the difficulty of comparing data between independent laboratories. Here, we propose a high-resolution typing method based on variable number tandem repeats (VNTRs) of genetic elements named mycobacterial interspersed repetitive units (MIRUs) in 12 human minisatellite-like regions of the M. ***tuberculosis*** genome.

MIRU-VNTR profiles of 72 different M. ***tuberculosis*** isolates were established by PCR analysis of all 12 loci. From 2 to 8 MIRU-VNTR alleles were identified in the 12 regions in these strains, which corresponds to a potential of over 16 million different combinations, yielding a resolution power close to that of IS6110-RFLP. All epidemiologically related isolates tested were perfectly clustered by MIRU-VNTR typing, indicating that the stability of these MIRU-VNTRs is adequate to track outbreak episodes. The correlation between genetic relationships inferred from MIRU-VNTR and IS6110-RFLP typing was highly significant. Compared with IS6110-RFLP, high-resolution MIRU-VNTR typing has the considerable advantages of being fast, appropriate for all M. ***tuberculosis*** isolates, including strains that have a few IS6110 copies, and permitting easy and rapid comparison of results from independent laboratories. This typing method opens the way to the construction of digital global databases for molecular epidemiology studies of M. ***tuberculosis*** .

L2 ANSWER 8 OF 73 BIOSIS COPYRIGHT 2001 BIOSIS
AN 2001:277624 BIOSIS
DN PREV200100277624
TI A combination of two genetic markers is sufficient for restriction fragment length polymorphism typing of Mycobacterium ***tuberculosis*** complex in areas with a high incidence of ***tuberculosis*** .
AU Rasolofo-Razanamparany, Voahangy (1); Ramarokoto, Herimanana; Auregan, Guy; ***Gicquel, Brigitte*** ; Chanteau, Suzanne
CS (1) Unite Tuberculose, Institut Pasteur, 101, Antananarivo: vrasolof@pasteur.mg Madagascar
SO Journal of Clinical Microbiology, (April, 2001) Vol. 39, No. 4, pp. 1530-1535. print.
ISSN: 0095-1137.
DT Article
LA English
SL English
AB The incidence of ***tuberculosis*** (TB) in Madagascar is 150 cases per 100,000 people. Because of this endemicity, we studied the genetic diversity of Mycobacterium ***tuberculosis*** strains isolated in four big cities in 1994 to 1995 with the aim of monitoring TB transmission. Isolates from 316 cases of pulmonary TB (PTM+) were typed by Southern hybridization with genetic markers IS6110 and DR. Of the 316 PTM+ strains, 66 (20.8%) had a single IS6110 band and were differentiated by the DR marker into 33 profiles. Using both markers, 37.7% (119) of the patients were clustered, a proportion similar to that in countries with a high prevalence of TB. There was no significant difference between clustered and nonclustered patients in age, sex, Mycobacterium bovis BCG status, and drug susceptibility of strains. Clustering was significantly greater in the capital, Antananarivo, than in the other cities, suggesting a higher rate of transmission. However, most of the patients in clusters were living in different areas, and, within a distance of 0.7 km, we did not find epidemiologically unrelated strains with the same restriction fragment length polymorphism profile. Despite an apparently low polymorphism, genetic markers such as IS6110 are potentially valuable for monitoring TB transmission. However, the high proportion of Malagasy isolates with a single IS6110 copy makes this marker alone unsuitable for typing. Additional markers such as DR are necessary for the differentiation of the isolates and for epidemiological surveys.

L2 ANSWER 9 OF 73 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 3
AN 2001:289670 BIOSIS
DN PREV200100289670
TI Isolation of strong expression signals of Mycobacterium ***tuberculosis*** .
AU Triccas, James A. (1); Britton, Warwick J.; ***Gicquel, Brigitte***
CS (1) Centenary Institute of Cancer Medicine and Cell Biology, Newtown, NSW, 2042: J.Triccas@centenary.usyd.edu.au Australia
SO Microbiology (Reading), (May, 2001) Vol. 147, No. 5, pp. 1253-1258. print.
ISSN: 1350-0872.
DT Article
LA English
SL English
AB The natural fluorescence of the Aequoria victoria green fluorescent protein was exploited to isolate strong expression signals of Mycobacterium ***tuberculosis*** . Mycobacterium bovis bacille Calmette-Guerin harbouring M. ***tuberculosis*** fragments driving high levels of gfp expression were isolated by fluorescence-activated cell sorting (FACS). DNA sequencing and subsequent comparison with the M. ***tuberculosis*** genome sequence revealed that a total of nine postulated promoters had been identified. The majority of the promoters displayed activity that was greater than or equal to the Mycobacterium fortuitum beta-lactamase promoter, one of the strongest mycobacterial promoters characterized to date. Two of the promoters corresponded to proteins predicted to be involved in calcium and magnesium utilization, the importance of such functions for cell physiology suggesting why these two genes are controlled by strong transcription signals. The seven other promoters corresponded to genes encoding proteins of unknown function. Promoter activity was maintained after prolonged incubation within macrophages, implying that these promoters could be used to drive sustained foreign gene expression in vivo. The strength of these expression signals identified could be employed for the overexpression of foreign genes in mycobacteria to aid protein purification and vaccine vector development. Furthermore, this study demonstrated that FACS provides a sensitive and efficient technique to measure and select strong mycobacterial expression signals.

L2 ANSWER 10 OF 73 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 4
AN 2001:141713 BIOSIS
DN PREV200100141713
TI Induction of neutralizing antibodies against diphtheria toxin by priming with recombinant Mycobacterium bovis BCG expressing CRM197, a mutant diphtheria toxin.
AU Miyaji, Eliane N. (1); Mazzantini, Rogerio P.; Dias, Waldely O.; Nascimento, Ana L. T. O.; Marcovistz, Rugimar; Matos, Denise S.; Raw, Isaias; Winter, Nathalie; ***Gicquel, Brigitte*** ; Rappuoli, Rino; Leite, Luciana C. C.
CS (1) Centro de Biotecnologia, Instituto Butantan, Av. Vital Brasil 1500, 05503-900, Sao Paulo, SP: enmiyaji@uol.com.br Brazil
SO Infection and Immunity, (February, 2001) Vol. 69, No. 2, pp. 869-874. print.
ISSN: 0019-9567.
DT Article
LA English
SL English

AB BCG, the attenuated strain of Mycobacterium bovis, has been widely used as a vaccine against ***tuberculosis*** and is thus an important candidate as a live carrier for multiple antigens. With the aim of developing a recombinant BCG (rBCG) vaccine against diphtheria, pertussis, and tetanus (DPT), we analyzed the potential of CRM197, a mutated nontoxic derivative of diphtheria toxin, as the recombinant antigen for a BCG-based vaccine against diphtheria. Expression of CRM197 in rBCG was achieved using Escherichia coli-mycobacterium shuttle vectors under the control of pBlaF*, an upregulated beta-lactamase promoter from Mycobacterium fortuitum. Immunization of mice with rBCG-CRM197 elicited an anti-diphtheria toxoid antibody response, but the sera of immunized mice were not able to neutralize diphtheria toxin (DTx) activity. On the other hand, a sub-immunizing dose of the conventional diphtheria-tetanus vaccine, administered in order to mimic an infection, showed that rBCG-CRM197 was able to prime the induction of a humoral response within shorter periods. Interestingly, the antibodies produced showed neutralizing activity only when the vaccines had been given as a mixture in combination with rBCG expressing tetanus toxin fragment C (FC), suggesting an adjuvant effect of rBCG-FC on the immune response induced by rBCG-CRM197. Isotype analysis of the anti-diphtheria toxoid antibodies induced by the combined vaccines, but not rBCG-CRM197 alone, showed an immunoglobulin G1-dominant profile, as did the conventional vaccine. Our results show that rBCG expressing CRM197 can elicit a neutralizing humoral response and encourage further studies on the development of a DPT vaccine with rBCG.

L2 ANSWER 11 OF 73 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 5
AN 2001:185607 BIOSIS
DN PREV200100185607
TI Method of selection of allelic exchange mutants.
AU Pelicic, Vladimir (1); Reyrat, Jean-Marc; ***Gicquel, Brigitte*** ; Guilhot, Christophe; Jackson, Mary
CS (1) Paris France
ASSIGNEE: Institut Pasteur, Paris, France
PI US 6096549 August 01, 2000
SO Official Gazette of the United States Patent and Trademark Office Patents, (Aug. 1, 2000) Vol. 1237, No. 1, pp. No Pagination. e-file. ISSN: 0098-1133.
DT Patent
LA English
AB A process for replacing a nucleotide sequence in the genome of a mycobacterium strain comprises the steps of: a) providing a vector containing SacB gene coding for levane saccharase enzyme and a nucleotide sequence of interest; b) transfecting the mycobacterium strain with the vector; c) selecting clones of the resulting transfected mycobacteria for replacement of the nucleotide sequence of interest by propagating the transfected clones in a culture medium supplemented with sucrose; and d) isolating the recombinant strain. The process is useful for positive selection of allelic exchange mutants, such as in Mycobacterium ***tuberculosis*** complex.

L2 ANSWER 12 OF 73 USPATFULL
AN 2000:1698 USPATFULL
TI Desaturase antigen of mycobacterium ***tuberculosis***
IN Jackson, Mary, Paris, France

Gicquel, Brigitte , Paris, France
PA Institut Pasteur, Paris, France (non-U.S. corporation)
PI US 6010855 20000104
AI US 1997-917299 19970725 (8)
PRAI US 1996-22713 19960726 (60)
DT Utility
EXNAM Primary Examiner: Achutamurthy, Ponnathapura; Assistant Examiner: Nashed, Nashaat T.
LREP Finnegan, Henderson, Farabow, Garrett & Dunner, L.L.P.
CLMN Number of Claims: 10
ECL Exemplary Claim: 1
DRWN 9 Drawing Figure(s); 12 Drawing Page(s)
LN.CNT 1192
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to the isolation of a new gene, des, which encodes a M. ***tuberculosis*** protein named DES. The des gene appears to be conserved among different Mycobacteria species. The amino acid sequence of the DES protein contains two sets of motifs that are characteristic of the active sites of enzymes from the class II diiron-oxo protein family. Among this family of proteins, DES shares significant homology with soluble stearoyl-ACP desaturases. DES is a highly antigenic protein, which is recognized by human sera from patients infected with M. ***tuberculosis*** and M. leprae but not by sera from tuberculous cattle. Thus, the DES protein provides a useful tool for the serodiagnostic analysis of ***tuberculosis*** .

L2 ANSWER 13 OF 73 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 6
AN 2000:455569 BIOSIS
DN PREV200000455569
TI Recombinant Mycobacterium bovis BCG expressing pertussis toxin subunit S1 induces protection against an intracerebral challenge with live Bordetella pertussis in mice.
AU Nascimento, Ivan P.; Dias, Waldely O.; Mazzantini, Rogerio P.; Miyaji, Eliane N.; Gamberini, Marcia; Quintilio, Wagner; Gebara, Vera C.; Cardoso, Diva F.; Ho, Paulo L.; Raw, Isaias; Winter, Nathalie; ***Gicquel,*** *** Brigitte*** ; Rappuoli, Rino; Leite, Luciana C. C. (1)
CS (1) Centro de Biotecnologia, Instituto Butantan, Av. Vital Brasil 1500, 05503-900, Sao Paulo, SP Brazil
SO Infection and Immunity, (September, 2000) Vol. 68, No. 9, pp. 4877-4883. print.
ISSN: 0019-9567.
DT Article
LA English
SL English
AB The recent development of acellular pertussis vaccines has been a significant improvement in the conventional whole-cell diphtheria-pertussis-tetanus toxoid vaccines, but high production costs will limit its widespread use in developing countries. Since Mycobacterium bovis BCG vaccination against ***tuberculosis*** is used in most developing countries, a recombinant BCG-pertussis vaccine could be a more viable alternative. We have constructed recombinant BCG (rBCG) strains expressing the genetically detoxified S1 subunit of pertussis toxin 9K/129G (S1PT) in fusion with either the beta-lactamase signal sequence or the whole beta-lactamase protein, under control of the upregulated M. fortuitum beta-lactamase promoter, pBlaF*. Expression levels were higher

in the fusion with the whole beta-lactamase protein, and both were localized to the mycobacterial cell wall. The expression vectors were relatively stable in vivo, since at two months 85% of the BCG recovered from the spleens of vaccinated mice maintained kanamycin resistance. Spleen cells from rBCG-S1PT-vaccinated mice showed elevated gamma interferon (IFN-gamma) and low interleukin-4 (IL-4) production, as well as increased proliferation, upon pertussis toxin (PT) stimulation, characterizing a strong antigen-specific Th1-dominant cellular response. The rBCG-S1PT strains induced a low humoral response against PT after 2 months. Mice immunized with rBCG-S1PT strains displayed high-level protection against an intracerebral challenge with live Bordetella pertussis, which correlated with the induction of a PT-specific cellular immune response, reinforcing the importance of cell-mediated immunity in the protection against B. pertussis infection. Our results suggest that rBCG-expressing pertussis antigens could constitute an effective, low-cost combined vaccine against ***tuberculosis*** and pertussis.

L2 ANSWER 14 OF 73 BIOSIS COPYRIGHT 2001 BIOSIS
AN 2001:46170 BIOSIS
DN PREV200100046170
TI Transmission of ***tuberculosis*** in the prison of Antananarivo (Madagascar.
AU Rasolofo-Razanamparany, Voahangy (1); Menard, Didier; Ratsitorahina, Mahery; Auregan, Guy; ***Gicquel, Brigitte*** ; Chanteau, Suzanne
CS (1) Unite tuberculose, Institut Pasteur, 101, Antananarivo: vrasolof@pasteur.mg Madagascar
SO Research in Microbiology, (November, 2000) Vol. 151, No. 9, pp. 785-795. print.
ISSN: 0923-2508.
DT Article
LA English
SL English
AB The prevalence of ***tuberculosis*** in the Antananarivo prison is 16 times higher than that in the general population of Madagascar. We compared the clustering of Mycobacterium ***tuberculosis*** strains within and outside the prison and studied the transmission of strains in the prison. M. ***tuberculosis*** strains isolated in 1994 to 1995 from 146 prisoners and from 260 nonprisoner patients from Antananaviro were typed using the genetic markers IS6110 and direct repeat. We compared the strains isolated from prisoners and nonprisoners and found that the clustering rate was higher within (58.9%) than outside the prison (40%) suggesting that the transmission rate was higher in prison. Of the 146 incarcerated patients, 82 were grouped into 22 clusters. We checked for possible ***tuberculosis*** transmission between prisoners with identical strains by epidemiological investigation of the various prison clusters. We found that 9.5% of the incarcerated patients could have been sources of infection and that only 15.1% could have been infected in the prison. One hundred and twenty-seven prison patients were new cases. Epidemiological data suggested that 37% of them resulted from a reactivation of an old infection, due to poor living conditions or recent transmission from an index case outside the prison.

L2 ANSWER 15 OF 73 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 7
AN 2000:305446 BIOSIS
DN PREV200000305446

TI Variable human minisatellite-like regions in the Mycobacterium ***tuberculosis*** genome.
AU Supply, Philip; Mazars, Edith; Lesjean, Sarah; Vincent, Veronique; ***Gicquel, Brigitte*** ; Locht, Camille
SO Molecular Microbiology, (May, 2000) Vol. 36, No. 3, pp. 762-771. print.
ISSN: 0950-382X.
DT Article
LA English
SL English
AB Mycobacterial interspersed repetitive units (MIRUs) are 40-100 bp DNA elements often found as tandem repeats and dispersed in intergenic regions of the Mycobacterium ***tuberculosis*** complex genomes. The M. ***tuberculosis*** H37Rv chromosome contains 41 MIRU loci. After polymerase chain reaction (PCR) and sequence analyses of these loci in 31 M. ***tuberculosis*** complex strains, 12 of them were found to display variations in tandem repeat copy numbers and, in most cases, sequence variations between repeat units as well. These features are reminiscent of those of certain human variable minisatellites. Of the 12 variable loci, only one was found to vary among genealogically distant BCG substrains, suggesting that these interspersed bacterial minisatellite-like structures evolve slowly in mycobacterial populations.

L2 ANSWER 16 OF 73 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 8
AN 2000:431772 BIOSIS
DN PREV200000431772
TI Life on the inside: Probing Mycobacterium ***tuberculosis*** gene expression during infection.
AU Triccas, James A. (1); ***Gicquel, Brigitte***
CS (1) Centenary Institute of Cancer Medicine and Cell Biology, Newtown, NSW, 2042 Australia
SO Immunology and Cell Biology, (August, 2000) Vol. 78, No. 4, pp. 311-317. print.
ISSN: 0818-9641.
DT Article
LA English
SL English
AB The identification of Mycobacterium ***tuberculosis*** genes specifically expressed during infection is a key step in understanding mycobacterial pathogenesis. Such genes most likely encode products required for survival within the host and for progressive infection. Recent advances in mycobacterial genetics have permitted the development of new techniques and the adaptation of existing methods to analyse mycobacterial in vivo gene expression and virulence. This has revealed a subset of M. ***tuberculosis*** genes that are differentially expressed during infection and has demonstrated that a number of components contribute to the virulence of the organism. This information is expected to provide new strategies to prevent ***tuberculosis*** infection, new targets for antimicrobial therapy and new insights into the infectious process.

L2 ANSWER 17 OF 73 CAPLUS COPYRIGHT 2001 ACS
AN 2000:517720 CAPLUS
DN 134:97544
TI Genetics of mycobacterial virulence
AU Collins, Desmond M.; ***Gicquel, Brigitte***

CS AgResearch, Wallaceville Animal Research Centre, Upper Hutt, N. Z.
SO Mol. Genet. Mycobact. (2000), 265-278. Editor(s): Hatfull, Graham F.; Jacobs, William R., Jr. Publisher: American Society for Microbiology, Washington, D. C.
CODEN: 69AEPU
DT Conference; General Review
LA English
AB A review with 110 refs. is presented regarding the genetics of mycobacterial virulence. Topics discussed include mycobacterial pathogenicity, the relation between virulence and Koch's mol. postulates, techniques for identifying candidate virulence genes, methods for detg. the virulence role of candidate genes, the role of particular genes in virulence, and virulence in mycobacteria other than the M. ***tuberculosis*** complex.
RE.CNT 110
RE
(1) Altare, F; Curr Opin Immunol 1998, V10, P413 CAPLUS
(2) Andersen, P; Scand J Immunol 1997, V45, P115 CAPLUS
(5) Arruda, S; Science 1993, V261, P1454 CAPLUS
(6) Azad, A; J Biol Chem 1997, V272, P16741 CAPLUS
(8) Balasubramanian, V; J Bacteriol 1996, V178, P273 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 18 OF 73 CAPLUS COPYRIGHT 2001 ACS
AN 1999:139976 CAPLUS
DN 130:205949
TI Proteins exported from mycobacteria, vectors comprising same and uses for diagnosing and preventing ***tuberculosis***
IN ***Gicquel, Brigitte*** ; Portnoi, Denis; Lim, Eng-Mong; Pelicic, Vladimir; Guigueno, Agnes; Goguet De La Salmoniere, Yves
PA Institut Pasteur, Fr.
SO PCT Int. Appl., 309 pp.
CODEN: PIXXD2
DT Patent
LA French
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9909186	A2	19990225	WO 1998-FR1813	19980814
WO 9909186	A3	19990805		
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
FR 2767336	A1	19990219	FR 1997-10404	19970814
FR 2767336	B1	20010518		
FR 2767337	A1	19990219	FR 1997-11325	19970911
AU 9890765	A1	19990308	AU 1998-90765	19980814
EP 1003888	A2	20000531	EP 1998-942748	19980814
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

PRAI FR 1997-10404 A 19970814
FR 1997-11325 A 19970911
WO 1998-FR1813 W 19980814

AB The invention concerns recombinant vectors which replicate in mycobacteria and can be used for screening for genes for exported proteins and a set of sequences coding for exported proteins detected by fusion with alk. phosphatase, in particular one polypeptide, called DP428, of about 12 kD corresponding to an exported protein found in mycobacteria belonging to the Mycobacterium ***tuberculosis*** complex. The invention also concerns methods and kits for detecting in vitro the presence of a mycobacterium and in particular a mycobacterium belonging to the Mycobacterium ***tuberculosis*** complex in a biol. sample using said polypeptides, their fragments or polynucleotides coding for the latter. The invention also concerns immunogenic or vaccine compns. for preventing and/or treating infections caused by mycobacteria and in particular a mycobacterium belonging to said complex, particularly ***tuberculosis***
.

L2 ANSWER 19 OF 73 CAPLUS COPYRIGHT 2001 ACS
AN 1999:96265 CAPLUS
DN 130:165435
TI Mycobacterium strain with modified erp gene and vaccine composition containing the same
IN ***Gicquel, Brigitte*** ; Berthet, Francois-Xavier
PA Institut Pasteur, Fr.
SO PCT Int. Appl., 53 pp.
CODEN: PIXXD2
DT Patent
LA French
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9905168	A1	19990204	WO 1998-FR1627	19980722
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
FR 2766495	A1	19990129	FR 1997-9303	19970722
AU 9888671	A1	19990216	AU 1998-88671	19980722
EP 991663	A1	20000412	EP 1998-940318	19980722
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

PRAI FR 1997-9303 19970722
WO 1998-FR1627 19980722

AB The invention concerns Mycobacterium strains whereof the erp gene is modified and a vaccine compn. contg. same. The modification of the erp gene decreases the virulence and the persistence of the Mycobacterium strains.

RE.CNT 6
RE
(1) Berthet, F; Microbiology 1995, V141(9), P2123 CAPLUS

(2) Lim, E; Journal of Bacteriology 1995, V177(1), P59 CAPLUS
(3) Pasteur Institut; WO 9607745 A 1996 CAPLUS
(4) Pasteur Institut; WO 9623885 A 1996 CAPLUS
(5) Pelicic, V; FEMS Microbiology Letters 1996, V144, P161 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 20 OF 73 CAPLUS COPYRIGHT 2001 ACS
AN 1999:77692 CAPLUS
DN 130:165432
TI The antigenic protein LHP of Mycobacterium ***tuberculosis*** and the lhp gene encoding it and their diagnostic and prophylactic uses
IN ***Gicquel, Brigitte*** ; Berthet, Francois-Xavier; Andersen, Peter; Rasmussen, Peter Birk
PA Institut Pasteur, Fr.; Statens Serum Institut
SO PCT Int. Appl., 88 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9904005	A1	19990128	WO 1998-IB1091	19980716
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9881238	A1	19990210	AU 1998-81238	19980716
EP 1003870	A1	20000531	EP 1998-930967	19980716
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

PRAI US 1997-52631 P 19970716
WO 1998-IB1091 W 19980716
AB The Mycobacterium ***tuberculosis*** gene encoding the antigenic protein LHP that is homologous to the L45 antigen of M. bovis, is cloned and characterized. The gene can be expressed from its own promoter in slow-growing (M. ***tuberculosis*** group) and fast-growing (M. smegmatis) mycobacteria. The LHP gene product, and antigenic peptides derived from it, can be manufd. for use in vaccines and to raise reagent antibodies for diagnostic use. The promoter of the lhp gene may be of use in the expression of foreign genes in Mycobacteria. Oligonucleotides derived from the promoter region may be useful as probes or primers in the detection of M. ***tuberculosis*** in a biol. sample. Anal. of the promoters driving expression of the closely linked lhp and orf1C genes of M. ***tuberculosis*** established that they form an operon. Use of the promoter to drive expression of a reporter gene in M. smegmatis is demonstrated. The protein is abundant in short-term (7 day) culture filtrates of M. ***tuberculosis*** .
RE.CNT 9
RE
(1) Ajinomoto Kk; EP 0400973 A 1990 CAPLUS
(3) Corixa Corp; WO 9709428 A 1997 CAPLUS

(4) Corixa Corp; WO 9709429 A 1997 CAPLUS
(5) Corixa Corp; WO 9816645 A 1998 CAPLUS
(6) Corixa Corp; WO 9816646 A 1998 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 21 OF 73 USPATFULL
AN 1999:128431 USPATFULL
TI Promoter of M. paratuberculosis and its use for the expression of immunogenic sequences
IN Murray, Alan, Palmerston North, New Zealand
Gheorghiu, Marina, Neuilly-Sur-Seine, France
Gicquel, Brigitte , Paris, France
PA Institut Pasteur, Paris Cedex, France (non-U.S. corporation)
Massey University, Palmerston North, New Zealand (non-U.S. corporation)
PI US 5968815 19991019
WO 9308284 19930429
AI US 1994-211718 19941006 (8)
WO 1992-EP2431 19921023
19941006 PCT 371 date
19941006 PCT 102(e) date
PRAI FR 1991-13227 19911025
DT Utility
EXNAM Primary Examiner: Guzo, David; Assistant Examiner: Degen, Nancy J.
LREP Oblon, Spivak, McClelland, Maier & Neustadt, P.C.
CLMN Number of Claims: 45
ECL Exemplary Claim: 1
DRWN 54 Drawing Figure(s); 50 Drawing Page(s)
LN.CNT 1643
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention relates to a nucleotide sequence which is present at a position adjacent to the 5' end of the reverse sequence complementary to the open reading frame coding for a potential transposase contained in the insertion element IS900 in Mycobacterium paratuberculosis. The nucleotide sequence has promoter functions and contains important signals for the regulation of transcription and translation. The invention also relates to methods for cloning and expressing heterologous proteins using such regulatory sequences, to vectors and transformed host cells containing these sequences, and to immunogenic compositions prepared by expression of nucleotide sequences placed under control of these regulatory sequences.

L2 ANSWER 22 OF 73 USPATFULL
AN 1999:27731 USPATFULL
TI Peptides encoded by nuclease sequences of actinomycetales and application as immunogenic compositions
IN Hance, Allan Johnson, Paris, France
Grandchamp-Desraux, Bernard, Paris, France
Levy-Frebault, Veronique, Paris, France
Gicquel, Brigitte , Paris, France
PA Institut National de la Sante et de la Recherche Mediale-Inserm & Institute Pasteur, Paris, France (non-U.S. corporation)
PI US 5877273 19990302
AI US 1995-473020 19950606 (8)
RLI Division of Ser. No. US 1991-623729, filed on 11 Feb 1991
PRAI FR 1989-5057 19890417

DT Utility
EXNAM Primary Examiner: Marschel, Ardin H.; Assistant Examiner: Riley, Jezian
LREP Dreger, Walter H., Brunelle, Jan P.
CLMN Number of Claims: 27
ECL Exemplary Claim: 1
DRWN 11 Drawing Figure(s); 9 Drawing Page(s)
LN.CNT 1176
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to nucleotide sequences of Actinomycetales, in particular of mycobacteria, to oligonucleotides contained within said nucleotide sequences, to their uses as primers for the synthesis of Actinomycetales DNA and as probes for the detection of DNA and/or the transcription products of Actinomycetales, in particular of mycobacteria, to the products of expression of said sequences, to their uses and to antibodies directed towards the said products, to a method for detecting and identifying Actinomycetales and its uses, as well as to immunogenic compositions comprising the said expression products.

L2 ANSWER 23 OF 73 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 9
AN 1999:527380 BIOSIS
DN PREV199900527380
TI Use of fluorescence induction and sucrose counterselection to identify Mycobacterium ***tuberculosis*** genes expressed within host cells.
AU Triccas, James A.; Berthet, Francois-Xavier; Pelicic, Vladimir; ***Gicquel, Brigitte (1)***
CS (1) Unite de Genetique Mycobacterienne, Institut Pasteur, 25 rue du Dr Roux, 75724, Paris Cedex 15 France
SO Microbiology (Reading), (Oct., 1999) Vol. 145, No. 10, pp. 2923-2930. ISSN: 1350-0872.
DT Article
LA English
SL English
AB The identification of Mycobacterium ***tuberculosis*** genes expressed within host cells would contribute greatly to the development of new strategies to combat ***tuberculosis*** . By combining the natural fluorescence of the Aequoria victoria green fluorescent protein (GFP) with the counterselectable property of the Bacillus subtilis SacB protein, M. ***tuberculosis*** promoters displaying enhanced in vivo activity have been isolated. Macrophages were infected with recombinant Mycobacterium bovis bacille Calmette-Guerin containing a library of M. ***tuberculosis*** promoters controlling gfp and sacB expression, and fluorescent bacteria recovered by fluorescence-activated cell sorting. The expression of sacB was used to eliminate clones with strong promoter activity outside the macrophage, resulting in the isolation of seven clones containing M. ***tuberculosis*** promoters with greater activity intracellularly. The gene products identified displayed similarity to proteins from other organisms whose functions include nutrient utilization, protection from oxidative stress and defence against xenobiotics. These proposed functions are consistent with conditions encountered within the host cell and thus suggest that the augmented activity of the isolated promoters/genes may represent strategies employed by M. ***tuberculosis*** to enhance intracellular survival and promote infection.

L2 ANSWER 24 OF 73 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 10
AN 1999:325863 BIOSIS
DN PREV199900325863
TI Persistence and protective efficacy of a Mycobacterium ***tuberculosis*** auxotroph vaccine.
AU Jackson, Mary (1); Phalen, Susan W.; Lagranderie, Micheline; Ensergueix, Danielle; Chavarot, Pierre; Marchal, Gilles; McMurray, David N.; ***Gicquel, Brigitte*** ; Guilhot, Christophe
CS (1) Unite de Genetique Mycobacterienne, Institut Pasteur, 25 rue du Dr. Roux, 75724, Paris cedex 15 France
SO Infection and Immunity, (June, 1999) Vol. 67, No. 6, pp. 2867-2873. ISSN: 0019-9567.
DT Article
LA English
SL English
AB New vaccines against ***tuberculosis*** are urgently required because of the impressive incidence of this disease worldwide and the highly variable protective efficacy of the current vaccine. The possibility of creating new live vaccines by the rational attenuation of strains from the Mycobacterium ***tuberculosis*** complex was investigated. Two auxotrophic mutants of M. ***tuberculosis*** and M. bovis BCG were constructed by disruption of one of their purine biosynthetic genes. These mutants appeared unable to multiply in vitro within mouse bone-marrow derived macrophages. They were also attenuated in vivo in the mouse and guinea pig animal models. In guinea pigs, the two mutants induced strong delayed-type hypersensitivity response to purified protein derivative. In a preliminary experiment, the two mutants were compared to the BCG vaccine for their protective efficacy in a challenge against aerosolized virulent M. ***tuberculosis*** in the guinea pig model. Both mutants conferred some level of protection. These experiments demonstrate that the rational attenuation of M. ***tuberculosis*** could lead to the design of new candidate live vaccines against ***tuberculosis*** .

L2 ANSWER 25 OF 73 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 11
AN 1999:396946 BIOSIS
DN PREV199900396946
TI A novel polymorphic genetic locus in members of the Mycobacterium ***tuberculosis*** complex.
AU Rauzier, Jean (1); Gormley, Eamonn; Gutierrez, M. Cristina; Kassa-Kelembho, Eric; Sandall, Laurie J.; Dupont, Chris; ***Gicquel,*** *** Brigitte*** ; Murray, Alan
CS (1) Unite de Genetique Mycobacterienne, Institut Pasteur, Paris France
SO Microbiology (Reading), (July, 1999) Vol. 145, No. 7, pp. 1695-1701. ISSN: 1350-0872.
DT Article
LA English
SL English
AB It has previously been shown that the PAN promoter from Mycobacterium paratuberculosis can be used as a DNA probe to identify an RFLP between wild-type Mycobacterium bovis and the vaccine strain Mycobacterium bovis BCG. To investigate the genetic basis of this phenomenon, DNA fragments from a New Zealand M. bovis cattle strain and M. bovis BCG Pasteur, containing the PAN-binding region, were isolated from gene libraries, sequenced and characterized. Sequence analysis and comparison with database sequences showed that the PAN region in M. bovis, M. bovis BCG

and Mycobacterium ***tuberculosis*** is identical and shares 70% similarity to the PAN sequence from M. paratuberculosis. The Shine-Dalgarno sequence and the -10 and -35 promoter regions are conserved between the different species. Analysis of the flanking sequences of the PAN region revealed that less than 1 kb downstream of PAN is a 2405 bp fragment that is present in M. bovis BCG but absent in the M. bovis wild-type strain. The distribution of the 2405 bp fragment in members of the M. ***tuberculosis*** complex was investigated and found to be present in 70 out of 70 M. ***tuberculosis*** strains, and 7 out of 7 M. bovis BCG daughter strains, 2 out of 2 Mycobacterium africanum strains, 2 out of 2 Mycobacterium microti strains and 7 out of 25 M. bovis strains. This is the first report of a genetic region of M. bovis BCG that is not universally present in M. bovis strains. The fragment does not appear to be present in any mycobacterial species outside the M. ***tuberculosis*** complex. It does not possess any characteristics of known transposable elements and the flanking sequences do not have any obvious features to suggest a deletion mechanism. The genetic location of this region is close to the 3' end of the RD1 region of M. bovis and M. ***tuberculosis*** . The polymorphic nature of this locus in M. bovis will provide an additional genetic marker for strain differentiation.

L2 ANSWER 26 OF 73 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 12
AN 1999:212167 BIOSIS
DN PREV199900212167
TI Inactivation of the antigen 85C gene profoundly affects the mycolate content and alters the permeability of the Mycobacterium ***tuberculosis*** cell envelope.
AU Jackson, Mary; Raynaud, Catherine; Laneelle, Marie-Antoinette; Guilhot, Christophe; Laurent-Winter, Christine; Ensergueix, Danielle; ***Gicquel,*** *** Brigitte*** ; Daffe, Mamadou (1)
CS (1) Institut de Pharmacologie et de Biologie Structurale du CNRS and Universite Paul Sabatier, 205, route de Narbonne, 31077, Toulouse cedex France
SO Molecular Microbiology, (March, 1999) Vol. 31, No. 5, pp. 1573-1587. ISSN: 0950-382X.
DT Article
LA English
AB The antigen 85 complex of Mycobacterium ***tuberculosis*** consists of three abundantly secreted proteins. The recent characterization of a mycoloyltransferase activity associated in vitro with each of these antigens suggested that they are potentially important for the building of the unusual cell envelope of mycobacteria. To define the physiological role of these proteins, the gene coding for antigen 85C was inactivated by transposon mutagenesis. The resulting mutant was shown to transfer 40% fewer mycolates to the cell wall with no change in the types of mycolates esterifying arabinogalactan or in the composition of non-covalently linked mycolates. As a consequence, the diffusion of the hydrophobic chenodeoxycholate and the hydrophilic glycerol, but not that of isoniazid, was found to be much faster through the cell envelope of the mutant than that of the parent strain. Taken together, these data demonstrate that: (i) antigen 85C is involved directly or indirectly in the transfer of mycolates onto the cell wall of the whole bacterium; (ii) the enzyme is not specific for a given type of mycolate; and (iii) the cell wall-linked mycolate layer may represent a barrier for the diffusion of small hydrophobic and hydrophilic molecules.

L2 ANSWER 27 OF 73 BIOSIS COPYRIGHT 2001 BIOSIS
AN 2000:77184 BIOSIS
DN PREV200000077184
TI Characterization of M. ***tuberculosis*** strains from West African patients by spoligotyping.
AU Niang, Mbayame Ndiaye (1); de la Salmoniere, Yves Goguet; Samb, Abibou; Hane, Abdoul Almamy; Cisse, Moussa Fafa; ***Gicquel, Brigitte*** ; Perraut, Ronald
CS (1) Laboratoire d'Immunologie, Institut Pasteur de Dakar, 36 Av. Pasteur, Dakar Senegal
SO Microbes and Infection, (Dec., 1999) Vol. 1, No. 14, pp. 1189-1192. ISSN: 1286-4579.
DT Article
LA English
SL English
AB Analysis of Mycobacterium ***tuberculosis*** strains was carried out using isolates collected from 69 Senegalese and 20 Ivory Coast ***tuberculosis*** patients. These 89 isolates were typed by means of the spoligotyping technique, showing clusterized populations of bacterial strains. In the Senegalese patients, 35 genetic profiles were observed with 10 clusters of spoligotypes from 44 isolates. Among Ivory Coast patients, 11 spoligotypes were found for 20 isolates. A particular cluster of isolates was evident both in Senegalese (10) and Ivory Coast (11) patients. These results show the existence of polymorphism of the direct repeat region for African M. ***tuberculosis*** strains. However they suggest that additionnal markers are needed for accurate epidemiological studies in areas that are highly endemic for ***tuberculosis*** .

L2 ANSWER 28 OF 73 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 13
AN 1999:509913 BIOSIS
DN PREV199900509913
TI Identification of a virulence gene cluster of Mycobacterium ***tuberculosis*** by signature-tagged transposon mutagenesis.
AU Camacho, Luis Reinaldo; Ensergueix, Danielle; Perez, Esther; ***Gicquel,*** *** Brigitte*** ; Guilhot, Christophe (1)
CS (1) Unite de Genetique Mycobacterienne, Institut Pasteur, 25 rue du Dr Roux, 75724, Paris Cedex 15 France
SO Molecular Microbiology, (Oct., 1999) Vol. 34, No. 2, pp. 257-267. ISSN: 0950-382X.
DT Article
LA English
SL English
AB ***Tuberculosis*** remains the greatest cause of death worldwide due to a single pathogen. In order to identify the genes required for the pathogenicity of Mycobacterium ***tuberculosis*** , a functional genomic approach was developed. A library of signature-tagged transposon mutants of this bacterium was constructed and screened for those affected in their multiplication within the lungs of mice. From 1927 mutants tested, 16 were attenuated for their virulence. The insertions harboured by the selected mutants were mapped on the M. ***tuberculosis*** genome and most of the mutated loci appeared to be involved in lipid metabolism or transport across the membrane. Four independent mutations identified a cluster of virulence genes located on a 50 kb chromosomal region. These genes might be involved in the production of phthiocerol and

phenolphthiocerol derivatives, a group of molecules restricted to eight mycobacterial species, seven of them being either strict or opportunistic pathogens. The interaction of five mutant strains with mouse bone marrow macrophages was investigated. These five mutants were still able to multiply in this cell type. However, in three cases, there was a growth defect in comparison with the wild-type strain. The other two strains exhibited no clear difference from the virulent strain, MT103, in this model. This study, which is the first global research of virulence factors of M. ***tuberculosis*** , opens the way to a better understanding of the molecules that are key players in the interaction of this pathogen with its host.

L2 ANSWER 29 OF 73 BIOSIS COPYRIGHT 2001 BIOSIS
AN 1999:435061 BIOSIS
DN PREV199900435061
TI Cytokine transcripts in pediatric ***tuberculosis*** : A study with bronchoalveolar cells.
AU Aubert-Pivert, Elisabeth (1); Chedevergne, Frederique; Lopez-Ramirez, Gloria (1); Colle, Jean-Herve; Scheinmann, Pierre; ***Gicquel, Brigitte*** *** (1)*** ; de Blic, Jacques
CS (1) Unite de Genetique Mycobacterienne, Institut Pasteur, Paris France
SO Journal of Interferon and Cytokine Research, (Sept., 1999) Vol. 19, No. SUPPL. 1, pp. S157.
Meeting Info.: Meeting of the International Society for Interferon and Cytokine Research with the participation of the European Cytokine Society Paris, France September 5-9, 1999 European Cytokine Society
. ISSN: 1079-9907.
DT Conference
LA English

L2 ANSWER 30 OF 73 CAPLUS COPYRIGHT 2001 ACS
AN 1999:8134 CAPLUS
DN 130:62000
TI Attenuated recombinant mycobacteria useful as immunogens or as vaccine components with therapeutic applications for ***tuberculosis***
IN ***Gicquel, Brigitte*** ; Guilhot, Christophe; Jackson, Mary
PA Institut Pasteur, Fr.
SO PCT Int. Appl., 74 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9856931	A1	19981217	WO 1998-IB898	19980611
W: CA, JP, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
EP 991767	A1	20000412	EP 1998-922986	19980611
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

PRAI US 1997-49390 19970611
WO 1998-IB898 19980611
AB The present invention relates to a recombinant mycobacterium strain of pathogenic origin capable of replicating in a macrophage of a host, said

strain contg. in its chromosome or on a plasmid a counterpart to a gene in the wild type mycobacterium coding for a protein necessary for the biosynthesis of a purine or a pyrimidine base, wherein said counterpart gene in the recombinant mycobacterium has been inactivated and to vector contg. a conditional lethal counter-selective marker gene, particularly the SacB gene and a nucleotide sequence consisting of an inactivated gene coding for a protein necessary for the biosynthesis of a purine or a pyrimidine base. Here a simple method is introduced for mutagenesis by allele exchange. The invention further relates to methods for producing said recombinant mycobacterium strain, and to immunogenic, vaccines and immunotherapeutic compns. comprising said alive or dead recombinant mycobacterium strain, for the prevention or the treatment of ***tuberculosis*** . Specifically, with the goal of developing a novel vaccine against ***tuberculosis*** , purC auxotrophic mutant strains carrying a defect in their purine biosynthetic pathway were constructed and their attenuation and protective efficacy were evaluated.

RE.CNT 6

RE

(1) Jackson, M; MICROBIOLOGY 1996, V142(9), P2439 CAPLUS
(2) Pasteur Institut Fr; EP 0812918 A 1997 CAPLUS
(4) Pelicic, V; MOLECULAR MICROBIOLOGY 1996, V20(5), P919 CAPLUS
(5) Pelicic, V; PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF USA 1997, V94(20), P10955 CAPLUS
(6) Whitehead Institute For Biomedical Research Us; WO 9503417 A 1995 CAPLUS

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 31 OF 73 CAPLUS COPYRIGHT 2001 ACS

AN 1998:106024 CAPLUS

DN 128:179358

TI DES protein antigen of Mycobacterium ***tuberculosis*** and its use as an immunodominant target for the humoral response of tuberculous patients

IN Jackson, Mary; ***Gicquel, Brigitte***

PA Institut Pasteur, Fr.; Jackson, Mary; Gicquel, Brigitte

SO PCT Int. Appl., 33 pp.
CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9804711	A2	19980205	WO 1997-IB923	19970725
WO 9804711	A3	19980423		
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9734562	A1	19980220	AU 1997-34562	19970725
US 6010855	A	20000104	US 1997-917299	19970725
EP 1007688	A2	20000614	EP 1997-930698	19970725
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

JP 2001500004 T2 20010109 JP 1998-508649 19970725
US 6204038 B1 20010320 US 1999-422662 19991022
PRAI US 1996-22713 P 19960726
US 1997-917299 A3 19970725
WO 1997-IB923 W 19970725
AB The use of genetic methodol. based on the fusion of the proteins with the alk. phosphatase allowed the isolation of a new exported protein of M. ***tuberculosis*** . Isolation of a gene encoding this exported protein called DES is described as well as its characterization and its distribution among the different mycobacterial species. The protein has in its primary sequence amino acids only found at the level of active sites of enzymes of class II diiron-oxo proteins family. Among the proteins of this family, DES protein of M. ***tuberculosis*** does not present significative homologies with stearoyl ACP desaturases. Secondly, the antigenic feature of this protein were studied. For this, DES protein of M. ***tuberculosis*** was overexpressed in Escherichia coli under recombinant and purified protein form from this bacterium. The reactivity of tuberculous patients sera infected by M. ***tuberculosis*** or M. bovis against DES protein in Western blot expts. was tested, and 100% of the tested patients shown to recognize the protein. The intensity of the antibody response against DES protein measured by ELISA of tuberculous patients sera compared with the one relating to sera patients suffering from other pathologies show that there is a significative difference between the intensity of the antibody responses of these 2 categories of patients. Accordingly, DES protein is a potentially interesting tool for the ***tuberculosis*** serodiagnostic.

L2 ANSWER 32 OF 73 USPATFULL
AN 1998:150681 USPATFULL
TI Method of selection of allelic exchange mutants
IN Pelicic, Vladimir, Paris, France
Reyrat, Jean-Marc, Paris, France
Gicquel, Brigitte , Paris, France
PA Institut Pasteur, Paris, France (non-U.S. corporation)
PI US 5843664 19981201
AI US 1996-661658 19960611 (8)
DT Utility
EXNAM Primary Examiner: Elliott, George C.; Assistant Examiner: Schwartzman, Robert
LREP Finnegan, Henderson, Farabow, Garrett & Dunner, L.L.P.
CLMN Number of Claims: 26
ECL Exemplary Claim: 1
DRWN 12 Drawing Figure(s); 12 Drawing Page(s)
LN.CNT 961
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A process for replacing a nucleotide sequence in the genome of a mycobacterium strain comprises the steps of:

a) providing a vector containing SacB gene coding for levane saccharase enzyme and a nucleotide sequence of interest;

b) transfecting the mycobacterium strain with the vector;

c) selecting clones of the resulting transfected mycobacteria for replacement of the nucleotide sequence of interest by propagating the

transfected clones in a culture medium supplemented with sucrose; and

d) isolating the recombinant strain.

The process is useful for positive selection of allelic exchange mutants, such as in Mycobacterium ***tuberculosis*** complex.

L2 ANSWER 33 OF 73 USPATFULL
AN 1998:143860 USPATFULL
TI Mycobacterial nucleic acid hybridization probes and methods of use
IN Guesdon, Jean-Luc, Paris, France
Thierry, Dominique, Boulogne, France
Ullmann, Agnes, Paris, France
Gicquel, Brigitte , Paris, France
Brisson-Noel, Anne, Paris, France
PA Institut Pasteur, Paris, France (non-U.S. corporation)
PI US 5837455 19981117
AI US 1995-487645 19950607 (8)
RLI Continuation of Ser. No. US 1992-829016, filed on 14 Apr 1992, now patented, Pat. No. US 5597911
PRAI FR 1989-11665 19890906
FR 1990-2676 19900302
DT Utility
EXNAM Primary Examiner: Horlick, Kenneth R.; Assistant Examiner: Tung, Joyce
LREP Oblon, Spivak, McClelland, Maier & Neustadt, P.C.
CLMN Number of Claims: 11
ECL Exemplary Claim: 1
DRWN 11 Drawing Figure(s); 11 Drawing Page(s)
LN.CNT 1132
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Fragments of nucleic acids derived from an appropriate mycobacteria genome, particularly Mycobacterium ***tuberculosis*** , their applications in the diagnosis of mycobacteria infections, as well as plasmides containing said fragments. The nucleotidic sequence is comprised of a nucleotidic sequence repeated in the genome of a mycobacterium and specific of the bacillus of ***tuberculosis*** and is characterized by a strong hybridation with M. ***tuberculosis*** .

L2 ANSWER 34 OF 73 USPATFULL
AN 1998:134621 USPATFULL
TI Recombinant beta-lactamase, usable as carrier molecule in immunogenic compositions
IN ***Gicquel, Brigitte*** , Paris, France
Timm, Juliano, Paris, France
Trias, Joaquim, San Mateo, CA, United States
Duez, Colette, Angleur, Belgium
Perilli, Maria-Grazia, L'Aquilie, Italy
Dusart, Jean, Nandrin, Belgium
Frere, Jean-Marie, Nandrin, Belgium
PA Institut Pasteur, Paris Cedex, France (non-U.S. corporation)
PI US 5830457 19981103
WO 9317113 19930902
AI US 1994-284465 19941114 (8)
WO 1993-FR151 19930212
19941114 PCT 371 date

19941114 PCT 102(e) date
PRAI FR 1992-1713 19920214
DT Utility
EXNAM Primary Examiner: Wax, Robert A.; Assistant Examiner: Lau, Kawai
LREP Oblon, Spivak, McClelland, Maier & Neustadt, P.C.
CLMN Number of Claims: 40
ECL Exemplary Claim: 1
DRWN 20 Drawing Figure(s); 20 Drawing Page(s)
LN.CNT 1481
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to a nucleotide sequence characterized in that it is selected amongst the following nucleotide sequences: the sequence of the gene coding for a B-lactamase, or any part of said gene, particularly the sequence between nucleotides 1 and 394 containing the signals for expression of the gene, or the coding sequence comprising nucleotides 395 to 1274, or any sequence hybridizing under stringent conditions with the above sequence. Utilization of B-lactamase as a carrier protein for carrying heterolog epitopes for the preparation of vaccine compositions is also disclosed.

L2 ANSWER 35 OF 73 USPATFULL
AN 1998:122215 USPATFULL
TI Nucleotide sequences of actinomycetales, oligonucleotides of said sequences and their use for detecting the presence of actinomycetales
IN Hance, Allan Johnson, Paris, France
Grandchamp-Desraux, Bernard, Paris, France
Levy-Frebault, Veronique, Paris, France
Gicquel, Brigitte , Paris, France
PA Institut National de la Sante et de la Recherche Mediale-Inserm, Paris, France (non-U.S. government)
Institute Pasteur, Paris, France (non-U.S. corporation)
PI US 5817459 19981006
WO 9012875 19901101
AI US 1991-623729 19910211 (7)
WO 1990-FR274 19900413
19910211 PCT 371 date
19910211 PCT 102(e) date
PRAI FR 1989-5057 19890417
DT Utility
EXNAM Primary Examiner: Marschel, Ardin H.
LREP Flehr Hohbach Test Albritton & Herbert LLP, Dreger, Walter H., Brunelle, Jan P.
CLMN Number of Claims: 52
ECL Exemplary Claim: 1
DRWN 11 Drawing Figure(s); 9 Drawing Page(s)
LN.CNT 1228
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to nucleotide sequences of Actinomycetales, in particular of mycobacteria, to oligonucleotides contained within said nucleotide sequences, to their uses as primers for the synthesis of Actinomycetales DNA and as probes for the detection of DNA and/or the transcription products of Actinomycetales, in particular of mycobacteria, to the products of expression of said sequences, to their uses and to antibodies directed towards the said products, to a method for detecting and identifying Actinomycetales and its uses, as

well as to immunogenic compositions comprising the said expression products.

L2 ANSWER 36 OF 73 USPATFULL
AN 1998:111760 USPATFULL
TI Mycobacterial nucleic acid hybridization probes and methods of use
IN Guesdon, Jean-Luc, Paris, France
Thierry, Dominique, Boulogne, France
Ullman, Agnes, Paris, France
Gicquel, Brigitte , Paris, France
Brisson-Noel, Anne, Paris, France
PA Institut Pasteur, Paris, France (non-U.S. corporation)
PI US 5807672 19980915
AI US 1995-487651 19950607 (8)
RLI Continuation of Ser. No. US 1992-829016, filed on 14 Apr 1992, now patented, Pat. No. US 5597911
PRAI FR 1989-11665 19890906
FR 1990-2676 19900302
DT Utility
EXNAM Primary Examiner: Horlick, Kenneth R.; Assistant Examiner: Tung, Joyce
LREP Oblon, Spivak, McClelland, Maier & Neustadt, P.C.
CLMN Number of Claims: 21
ECL Exemplary Claim: 1
DRWN 9 Drawing Figure(s); 10 Drawing Page(s)
LN.CNT 1173
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Fragments of nucleic acids derived from an appropriate mycobacteria genome, particularly Mycobacterium ***tuberculosis*** , their applications in the diagnosis of mycobacteria infections, as well as plasmides containing said fragments. The nucleotidic sequence is comprised of a nucleotidic sequence repeated in the genome of a mycobacterium and specific of the bacillus of ***tuberculosis*** and is characterized by a strong hybridation with M. ***tuberculosis*** .

L2 ANSWER 37 OF 73 BIOSIS COPYRIGHT 2001 BIOSIS
AN 1998:432905 BIOSIS
DN PREV199800432905
TI Counterselectable markers: Untapped tools for bacterial genetics and pathogenesis.
AU Reyrat, Jean-Marc (1); Pelicic, Vladimir; ***Gicquel, Brigitte*** ; Rappuoli, Rino
CS (1) IRIS Chiron-Vaccines, Via Fiorentina 1, 53100 Siena Italy
SO Infection and Immunity, (Sept., 1998) Vol. 66, No. 9, pp. 4011-4017. ISSN: 0019-9567.
DT General Review
LA English

L2 ANSWER 38 OF 73 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 14
AN 1999:28278 BIOSIS
DN PREV199900028278
TI A Mycobacterium ***tuberculosis*** operon encoding ESAT-6 and a novel low-molecular-mass culture filtrate protein (CFP-10.
AU Berthet, Fancois-Xavier (1); Rasmusse, Peter Birk; Rosenkrands, Ida; Andersen, Peter; ***Gicquel, Brigitte***
CS (1) Unite Geneitque Mycobacteriene, Inst. Pasteur, 25 rue Dr Roux, 75724

Paris Cedex 15 France
SO Microbiology (Reading), (Nov., 1998) Vol. 144, No. 11, pp. 3195-3203. ISSN: 1350-0872.
DT Article
LA English
AB The early secreted antigenic target 6 kDa protein (ESAT-6) is a potent T-cell protein antigen synthesized by Mycobacterium ***tuberculosis*** . Its corresponding gene (esat-6) is located in RD1, a 10 kb DNA region deleted in the attenuated ***tuberculosis*** vaccine strain Mycobacterium bovis BCG. The promoter region of M. ***tuberculosis*** esat-6 was cloned and characterized. A new gene, designated lhp and cotranscribed with esat-6, was identified. Moreover, computer searches in the M. ***tuberculosis*** genome identified 13 genes related to the lhp/esat-6 operon, defining a novel gene family. The transcription initiation sites of the lhp/esat-6 operon were mapped using M. ***tuberculosis*** RNA. The corresponding promoter signals were not recognized in Mycobacterium smegmatis, in which transcription of lhp/esat-6 is initiated at different locations. The M. ***tuberculosis*** lhp gene product was identified as CFP-10, a low-molecular-mass protein found in the short-term culture filtrate. These results show that the genes encoding CFP-10 and ESAT-6 are transcribed together in M. ***tuberculosis*** and that both code for small exported proteins.

L2 ANSWER 39 OF 73 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 15
AN 1999:8627 BIOSIS
DN PREV199900008627
TI Attenuation of virulence by disruption of the Mycobacterium ***tuberculosis*** erp gene.
AU Berthet, Francois-Xavier (1); Lagranderie, Micheline; Gounon, Pierre; Laurent-Winter, Christine; Ensergueix, Danielle; Chavarot, Pierre; Thouron, Francoise; Maranghi, Eddie; Pelicic, Vladimir; Portnoi, Denis; Marchal, Gilles; ***Gicquel, Brigitte***
CS (1) Unite de Genetique Mycobacterienne, Institut Pasteur, 25 rue du Docteur Roux, 75724 Paris Cedex 15 France
SO Science (Washington D C), (Oct. 23, 1998) Vol. 282, No. 5389, pp. 759-762. ISSN: 0036-8075.
DT Article
LA English
AB The virulence of the mycobacteria that cause ***tuberculosis*** depends on their ability to multiply in mammalian hosts. Disruption of the bacterial erp gene, which encodes the exported repetitive protein, impaired multiplication of M. ***tuberculosis*** and M. bovis Bacille Calmette-Guerin in cultured macrophages and mice. Reintroduction of erp into the mutants restored their ability to multiply. These results indicate that erp contributes to the virulence of M. ***tuberculosis***
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L2 ANSWER 40 OF 73 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 16
AN 1998:404162 BIOSIS
DN PREV199800404162
TI Identification of genetic loci implicated in the survival of Mycobacterium smegmatis in human mononuclear phagocytes.
AU Lagier, Beatrice (1); Pelicic, Vladimir; Lecossier, Denise; Prod'hom, Guy; Rauzier, Jean; Guilhot, Christophe; ***Gicquel, Brigitte*** ; Hance,

Allan J.
CS (1) INSERM U82, Faculte de Medecine Xavier Bichat, Paris France
SO Molecular Microbiology, (July, 1998) Vol. 29, No. 2, pp. 465-475. ISSN: 0950-382X.
DT Article
LA English
AB A luminescence-based procedure that permits the rapid evaluation of the survival of mycobacteria within mononuclear phagocytes was developed and used to screen insertional mutants of Mycobacterium smegmatis for their ability to survive in human monocyte-derived macrophages. Among the 5000 mutants tested, eight mutants were identified that demonstrated impaired intracellular survival in human macrophages but that grew normally in the absence of cells. For each mutant, a portion of the gene interrupted by the transposition event was amplified by ligand-mediated PCR and sequenced. In all cases, the existence of homologous genes of as yet unknown function were identified in the Mycobacterium ***tuberculosis*** genome. Complementation of the mutant mycobacterial strains with cosmids containing the homologous loci from M. ***tuberculosis*** restored normal intracellular growth in three of the four mutants tested, supporting the idea that these loci contain genes that are important for intracellular survival. This study demonstrates the feasibility of directly screening mutant mycobacterial strains to identify genes coding for activities necessary for the intracellular survival in human mononuclear phagocytes, an important initial step in the identification of potential targets for new therapeutic agents.

L2 ANSWER 41 OF 73 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 17
AN 1998:270955 BIOSIS
DN PREV199800270955
TI Genetic advances for studying Mycobacterium ***tuberculosis*** pathogenicity.
AU Pelicic, Vladimir (1); Reyrat, Jean-Marc; ***Gicquel, Brigitte***
CS (1) Unite Genetique Mycobacterienne, Inst. Pasteur, 75724 Paris Cedex 15 France
SO Molecular Microbiology, (May, 1998) Vol. 28, No. 3, pp. 413-420. ISSN: 0950-382X.
DT General Review
LA English
AB ***Tuberculosis*** remains the greatest cause of death worldwide because of a single pathogen. Despite its importance, the genetic basis of the pathogenicity of Mycobacterium ***tuberculosis*** remains poorly understood, mainly because the most productive investigative approach, molecular genetic analysis, has been severely hampered by a lack of efficient tools. However, significant advances, including the development of methods for inactivating genes and studying their expression with reporter genes, have been recently made. This progress may lead to opportunities for developing new vaccines and antituberculous drugs. The aim of this review is to examine the present state of the art in mycobacterial molecular genetics and pinpoint some expected or promising areas for future research.

L2 ANSWER 42 OF 73 CAPLUS COPYRIGHT 2001 ACS
AN 1997:808084 CAPLUS
DN 128:136915
TI A reliable amplification technique for the characterization of genomic DNA

sequences flanking insertion sequences
AU Prod'hom, Guy; Lagier, Beatrice; Pelicic, Vladimir; Hance, Allan J.; ***Gicquel, Brigitte*** ; Guilhot, Christophe
CS Centre national de reference des mycobacteries, Institut Pasteur, Paris, Fr.
SO FEMS Microbiol. Lett. (1998), 158(1), 75-81
CODEN: FMLED7; ISSN: 0378-1097
PB Elsevier Science B.V.
DT Journal
LA English
AB A simple and efficient ligation-mediated PCR (LMPCR) is described for amplifying DNA adjacent to known sequences. The method uses one primer specific for the known sequence and a second specific for a synthetic linker ligated to restricted genomic DNA. Perkin-Elmer AmpliTaq Gold polymerase is used to minimize non-specific primer annealing and amplification. This LMPCR method was successfully applied to isolate DNA sequences flanking mobile elements present in mycobacterial mutants generated by transposon mutagenesis.

L2 ANSWER 43 OF 73 CAPLUS COPYRIGHT 2001 ACS
AN 1998:13732 CAPLUS
DN 128:71600
TI Method of selection of allelic exchange mutants of mycobacterium
IN Pelicic, Vladimir; Reyrat, Jean-marc; ***Gicquel, Brigitte*** ; Guilhot, Christophe; Jackson, Mary
PA Institut Pasteur, Fr.
SO Eur. Pat. Appl., 34 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI EP 812918	A2	19971217	EP 1997-401321	19970611
EP 812918	A3	19980422		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
US 5843664	A	19981201	US 1996-661658	19960611
CA 2208315	AA	19971211	CA 1997-2208315	19970611
AU 9724833	A1	19971218	AU 1997-24833	19970611
AU 728576	B2	20010111		
JP 10094397	A2	19980414	JP 1997-190376	19970611

PRAI US 1996-661658 A 19960611
AB A process for replacing a nucleotide sequence in the genome of a mycobacterium strain comprises the steps of: a) providing a vector contg. SacB gene coding for levane saccharase enzyme and a nucleotide sequence of interest; b) transfecting the mycobacterium strain with the vector; c) selecting clones of the resulting transfected mycobacteria for replacement of the nucleotide sequence of interest by propagating the transfected clones in a culture medium supplemented with sucrose; and d) isolating the recombinant strain. The process is useful for pos. selection of allelic exchange mutants, such as in Mycobacterium ***tuberculosis*** . SacB may be used for the pos. selection of mutants in either single-step or two-step selection strategies. In a single-step protocol, a suicide vector is electroporated into M. smegmatis and the allelic exchange

mutants are directly selected on sucrose. In a two-step selection, a single recombination transformant is first selected and propagated in liq. broth to allow a second crossing-over to occur. Then by plating on sucrose, the mutants that have lost the SacB gene during the second crossing-over can be pos. selected. In a two-step selection of ureC mutants of M. bovis BCG, a 6-fold increase in mutants was obtained relative to the one-step selection without sucrose.

L2 ANSWER 44 OF 73 USPATFULL
AN 97:8011 USPATFULL
TI Mycobacterial nucleic acid hybridization probes and methods of use
IN Guesdon, Jean-Luc, Paris, France
Thierry, Dominique, Boulogne, France
Ullmann, Agn es, Paris, France
Gicquel, Brigitte , Paris, France
Brisson-Noel, Anne, Parris, France
PA Institut Pasteur, Paris, France (non-U.S. corporation)
PI US 5597911 19970128
WO 9103558 19910321
AI US 1992-829016 19920414 (7)
WO 1990-FR591 19900906
19920414 PCT 371 date
19920414 PCT 102(e) date
PRAI FR 1989-11665 19890906
FR 1990-2676 19900302
DT Utility
EXNAM Primary Examiner: Jones, W. Gary; Assistant Examiner: Schreiber, David
LREP Oblon, Spivak, McClelland, Maier & Neustadt, P.C.
CLMN Number of Claims: 8
ECL Exemplary Claim: 1
DRWN 11 Drawing Figure(s); 11 Drawing Page(s)
LN.CNT 1140
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Nucleic acid fragments have been obtained from the genome of mycobacteria, and applications of the nucleic acid fragments in the diagnosis of mycobacterial infections are described. More particularly, the present invention concerns an isolated polynucleotide of the formula:

5'-(SEQ ID NO: 1)-(formula III)-(SEQ ID NO: 2)-3'

where formula III represents a polynucleotide containing nucleotides 343-1152 of SEQ ID NO: 3. Primers and probes based on the isolated polynucleotide, DNA complementary to any of the polynucleotides, primers or probes, a method of detecting and identifying at least one species or group of mycobacteria, and a kit, box, or coordinated set for conducting the method are also described.

L2 ANSWER 45 OF 73 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 18
AN 1997:488737 BIOSIS
DN PREV199799787940
TI Efficient allelic exchange and transposon mutagenesis in Mycobacterium ***tuberculosis*** .
AU Pelicic, Vladimir (1); Jackson, Mary; Reyrat, Jean-Marc; Jacobs., William R., Jr.; ***Gicquel, Brigitte*** ; Guilhot, Christophe

CS (1) Unite de Genetique Mycobacterienne, Inst. Pasteur, 25 rue du Dr. Roux, F-75724 Paris France
SO Proceedings of the National Academy of Sciences of the United States of America, (1997) Vol. 94, No. 20, pp. 10955-10960.
ISSN: 0027-8424.
DT Article
LA English
AB A better understanding of Mycobacterium ***tuberculosis*** virulence mechanisms is highly dependent on the design of efficient mutagenesis systems. A system enabling the positive selection of insertional mutants having lost the delivery vector was developed. It uses ts-sacB vectors, which combine the counterselective properties of the sacB gene and a mycobacterial thermosensitive origin of replication and can therefore be efficiently counterselected on sucrose at 39 degree C. This methodology allowed the construction of M. ***tuberculosis*** transposition mutant libraries. Greater than 10-6 mutants were obtained, far exceeding the number theoretically required to obtain at least one insertion in every nonessential gene. This system is also efficient for gene exchange mutagenesis as demonstrated with the purC gene: 100% of the selected clones were allelic exchange mutants. Therefore, a single, simple methodology has enabled us to develop powerful mutagenesis systems, the lack of which was a major obstacle to the genetic characterization of M. ***tuberculosis*** .

L2 ANSWER 46 OF 73 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 19
AN 1998:32248 BIOSIS
DN PREV199800032248
TI Rapid discrimination of Mycobacterium ***tuberculosis*** complex strains by ligation-mediated PCR fingerprint analysis.
AU Prod'hom, Guy; Guilhot, Christophe; Gutierrez, M. Cristina; Varnerot, Anne; ***Gicquel, Brigitte*** ; Vincent, Veronique (1)
CS (1) Cent. Natl. Reference Mycobacteries, Inst. Pasteur, Paris France
SO Journal of Clinical Microbiology, (Dec., 1997) Vol. 35, No. 12, pp. 3331-3334.
ISSN: 0095-1137.
DT Article
LA English
AB A ligation-mediated PCR (LMPCR) method for the amplification of sequences flanking the IS6110 of the Mycobacterium ***tuberculosis*** complex has been developed. The method uses one primer specific for IS6110 and a second specific for a linker ligated to SalI-restricted genomic DNA. LMPCR is a rapid screening method, valuable for the fingerprinting of M. ***tuberculosis*** complex strains.

L2 ANSWER 47 OF 73 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 20
AN 1997:345580 BIOSIS
DN PREV199799644783
TI Mycobacterium ***tuberculosis*** Des protein: An immunodominant target for the humoral response of tuberculous patients.
AU Jackson, Mary (1); Portnoi, Denis; Catheline, Daniel; Dumail, Laure; Rauzier, Jean; Legrand, Philippe; ***Gicquel, Brigitte***
CS (1) Unite de Genetique Mycobacterienne, Inst. Pasteur, 25 rue du Dr. Roux, 75724 Paris Cedex 15 France
SO Infection and Immunity, (1997) Vol. 65, No. 7, pp. 2883-2889.
ISSN: 0019-9567.

DT Article
LA English
AB The phoA gene fusion methodology permitted the identification of a new Mycobacterium ***tuberculosis*** exported protein, Des. This protein has significant sequence similarities to plant acyl-acyl carrier protein desaturases, which are enzymes involved in general fatty acid biosynthesis as well as in mycolic acid biosynthesis in mycobacteria. As shown by Western blot and enzyme-linked immunosorbent assay experiments, the Des protein is a major B-cell antigen that was recognized by all the tuberculous M. ***tuberculosis*** - and M. bovis-infected human patients tested.

L2 ANSWER 48 OF 73 BIOSIS COPYRIGHT 2001 BIOSIS
AN 1997:440259 BIOSIS
DN PREV199799739462
TI Evaluation of spoligotyping in a study of the transmission of Mycobacterium ***tuberculosis*** .
AU Goguet De La Salmoniere, Yves-Olivier (1); Li, Ho Minh; Torrea, Gabriela; Bunschoten, Annelies; Van Embden, Jan; ***Gicquel, Brigitte***
CS (1) Unite Genet. Mycobacterienne, Inst. Pastuer, 25 rue de Dr. Roux, 75724 Paris Cedex 15 France
SO Journal of Clinical Microbiology, (1997) Vol. 35, No. 9, pp. 2210-2214. ISSN: 0095-1137.
DT Article
LA English
AB Spoligotyping (for spacer oligotyping) is an easy, economical, and rapid way of typing Mycobacterium ***tuberculosis*** complex strains with the DR spacer markers (J. Kamerbeek et al., J. Clin. Microbiol. 35:907-914, 1997; D. van Soolingen et al., 33:3234-3248, 1995). The stability of the markers was demonstrated by showing that all the Mycobacterium bovis BCG strains tested gave the same spoligotyping pattern. None of the 42 atypical mycobacterial strains tested gave a spoligotyping signal, indicating the specificity of the technique for M. ***tuberculosis*** complex. The utility of the spoligotyping method was demonstrated by analyzing 106 isolates of M. ***tuberculosis*** obtained over 1 year in three Paris hospitals. The results obtained by this technique were compared to those obtained by Torrea et al. (G. Torrea et al., J. Clin. Microbiol. 34:1043-1049, 1996) by IS6110-based restriction fragment length polymorphism (RFLP) analysis. Strains from patients with epidemiological relationships that were in the same IS6110-RFLP cluster were also in the same spoligotyping group. Spoligotyping was more discriminative than RFLP analysis for strains with one or two copies of IS6110. RFLP analysis did not discriminate between the nine strains with one or two IS6110 bands with no known epidemiological relation, whereas spoligotyping distinguished between eight different types. IS6110-RFLP analysis split some of the spoligotyping clusters, particularly when the IS6110 copy number was high. Therefore, we propose a strategy for typing M. ***tuberculosis*** strains in which both markers are used.

L2 ANSWER 49 OF 73 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 21
AN 1997:295187 BIOSIS
DN PREV199799594390
TI Aminoglycoside 2'-N-acetyltransferase genes are universally present in mycobacteria: Characterization of the aac(2')-Ic gene from Mycobacterium

tuberculosis and the aac(2')-Id gene Mycobacterium smegmatis.
AU Ainsa, Jose A. (1); Perez, Esther; Pelicic, Vladimir; Berthet, Francois-Xavier; ***Gicquel, Brigitte*** ; Martin, Carlos
CS (1) Dep. Microbiol. Med. Preventiva Salud Publica, Fac. Med., Univ. Zaragoza, 50009-Zaragoza Spain
SO Molecular Microbiology, (1997) Vol. 24, No. 2, pp. 431-441. ISSN: 0950-382X.
DT Article
LA English
AB The genus Mycobacterium comprises clinically important pathogens such as M. ***tuberculosis*** , which has reemerged as a major cause of morbidity and mortality world-wide especially with the emergence of multi-drug-resistant strains. The use of fast-growing species such as Mycobacterium smegmatis has allowed important advances to be made in the field of mycobacterial genetics and in the study of the mechanisms of resistance in mycobacteria. The isolation of an aminoglycoside-resistance gene from Mycobacterium fortuitum has recently been described. The aac(2')-Ib gene is chromosomally encoded and is present in all isolates of M. fortuitum. The presence of this gene in other mycobacterial species is studied here and genes homologous to that of M. fortuitum have been found in all mycobacterial species studied. In this report, the cloning of the aac(2')-Ic gene from M. ***tuberculosis*** H37Rv and the aac(2')-Id gene from M. smegmatis mc-2155 is described. Southern blot hybridizations have shown that both genes are present in all strains of this species studied to date. In addition, the putative aac(2')-Ie gene has been located in a recent release of the Mycobacterium leprae genome. The expression of the aac(2')-Ic and aac(2')-Id genes has been studied in M. smegmatis and only aac(2')-Id is correlated with aminoglycoside resistance. In order to elucidate the role of the aminoglycoside 2'-N-acetyltransferase genes in mycobacteria and to determine whether they are silent resistance genes or whether they have a secondary role in mycobacterial metabolism, the aac(2')-Id gene from M. smegmatis has been disrupted in the chromosome of M. smegmatis mc-2155. The disruptant shows an increase in aminoglycoside susceptibility along with a slight increase in the susceptibility to lysozyme.

L2 ANSWER 50 OF 73 CAPLUS COPYRIGHT 2001 ACS
AN 1998:189506 CAPLUS
DN 128:279320
TI Genomic profile of Romanian M. ***tuberculosis*** strains appreciated by spoligotyping
AU Popa, M. I.; Goguet, Y.; Teodor, Irina; Popa, Loredana; Stefan, Mirela; Banica, Dorina; ***Gicquel, Brigitte***
CS Cantacuzino Institute, Bucharest, Rom.
SO Rom. Arch. Microbiol. Immunol. (1997), 56(1-2), 63-75 CODEN: RAMIE5; ISSN: 1220-8485
PB Institutul Cantacuzino
DT Journal
LA English
AB Within the present epidemiol. context and using new diagnostic methods and epidemiol. surveillance, we began evaluation of a new technique of mol. typing and obtained some preliminary data concerning the genomic profile of Romanian Mycobacterium ***tuberculosis*** strains. Spoligotyping (spacer oligonucleotide typing) is one of the most recent mol. typing methods (the first reviews on this procedure for characterizing M.

tuberculosis strains were published in 1997). We studied M. ***tuberculosis*** strains isolated in Romania. The strains were cultivated and tested through classical bacteriol. methods in the Cantacuzino Institute, Mycobacteria Antigens Lab. Transport was performed in a phosphate saline suspension, in cryoppt. tubes according to the present international regulations. The processing of the strains and the spoligotyping test was made at the Pasteur Institute in Paris. The present study is an attempt at detg. the genomic profile of some local M. ***tuberculosis*** strains in order to establish the utility of such a method in the conditions of our country. From the classical bacteriol. point of view the strains studied presented characteristics of M. ***tuberculosis*** (slow growing at 37.degree.C, rough, non-pigmented colony, pos. niacin producing test, nitrate redn. and growing on thiophene-2-carboxylic acid hydrazide media). This first test emphasized significant polymorphism of the Romanian M. ***tuberculosis*** strains even if though the no. of the strains studied was small and did not permit a rigorous statistical estn. The protocol is rapid, specific, and sensitive and the costs are smaller than RFLP study. Besides, compared to the RFLP, spoligotyping is less difficult and may be performed easily.

L2 ANSWER 51 OF 73 CAPLUS COPYRIGHT 2001 ACS
AN 1996:350332 CAPLUS
DN 125:27682
TI Cloning and expression vectors for mycobacterial hosts for detection of genes for secreted proteins
IN ***Gicquel, Brigitte*** ; Lim, Eng Mong; Portnoi, Denis; Berthet, Francois-Xavier; Timm, Juliano
PA Institut Pasteur, Fr.
SO PCT Int. Appl., 69 pp.
CODEN: PIXXD2
DT Patent
LA French
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9607745	A2	19960314	WO 1995-FR1133	19950830
W: CA, JP, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
FR 2724183	A1	19960308	FR 1994-10585	19940902
FR 2724183	B1	19970411		
CA 2197717	AA	19960314	CA 1995-2197717	19950830
EP 770138	A2	19970502	EP 1995-929147	19950830
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 10504966	T2	19980519	JP 1995-509250	19950830
US 6248581	B1	20010619	US 1997-793701	19970609
PRAI FR 1994-10585	A	19940902		
WO 1995-FR1133	W	19950830		

AB Cloning and expression vectors for identification of genes for secreted proteins of Mycobacteria have a replicon functional in a mycobacterium; a selectable marker; an expression cassette with a multiple cloning site and a transcription terminator. The expression cassette also has a sequence encoding a reporter moiety that lacks a promoter or signal sequence. When a gene for a secreted protein is cloned upstream of the reporter moiety, the distribution of the reporter activity can be used to identify membrane-bound or assocd. or secreted proteins. This vector is used for

identification and expression of exported polypeptides, such as the Mycobacterium ***tuberculosis*** P28 antigen for use in new vaccines against Mycobacteria. The use of the vectors is demonstrated by reconstruction expts. using the regulatory and signal regions of the blaF* gene of M. fortuitum to direct secretory expression of an alk. phosphatase (phoA) gene. The same construct was used to identify a no. of genes for secreted proteins of M. ***tuberculosis*** .

L2 ANSWER 52 OF 73 BIOSIS COPYRIGHT 2001 BIOSIS
AN 1996:462928 BIOSIS
DN PREV199699185284
TI Urease activity does not contribute dramatically to persistence of Mycobacterium bovis bacillus Calmette-Guerin.
AU Reyrat, Jean-Marc; Lopez-Ramirez, Gloria; Ofredo, Catherine; ***Gicquel,*** *** Brigitte*** ; Winter, Nathalie (1)
CS (1) Unite Genet. Mycobacterienne, Inst. Pasteur, 25 Dr. Roux, 75724 Paris Cedex 15 France
SO Infection and Immunity, (1996) Vol. 64, No. 9, pp. 3934-3936. ISSN: 0019-9567.
DT Article
LA English
AB Multiplication of BCGure-, an isogenic urease-negative mutant of Mycobacterium bovis BCG constructed by allelic exchange (J. M. Reyrat, F. X. Berthet, and B. Gicquel, Proc. Natl. Acad. Sci. USA 92:8768-8772, 1995), was examined in human macrophages and mice. Although ureolytic activity was not essential to BCGure-growth, a slight decrease in the multiplication and persistence of the mutated strain compared with wild-type BCG was observed in lungs of infected mice.

L2 ANSWER 53 OF 73 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 22
AN 1997:64816 BIOSIS
DN PREV199799364019
TI Physical mapping of Mycobacterium bovis BCG Pasteur reveals differences from the genome map of Mycobacterium ***tuberculosis*** H37Rv and from M. bovis.
AU Philipp, Wolfgang J.; Nair, Shamila; Guglielmi, Gerard; Lagranderie, Micheline; ***Gicquel, Brigitte*** ; Cole, Stewart T. (1)
CS (1) Unite Genetique Moleculaire Bacterienne, Institut Pasteur, 28 rue du Docteur Roux, 75724 Paris Cedex 15 France
SO Microbiology (Reading), (1996) Vol. 142, No. 11, pp. 3135-3145. ISSN: 1350-0872.
DT Article
LA English
AB A DraI restriction map of the apprx 4.35 Mb circular chromosome of the vaccine strain Mycobacterium bovis BCG Pasteur was constructed by linking all 21 DraI fragments, ranging in size from 6 to 820 kb, using specific clones that spanned the DraI recognition sites as hybridization probes. The positions of 20 known genes were also established. Comparison of the resultant genome map with that of the virulent tubercle bacillus Mycobacterium ***tuberculosis*** H37Rv revealed extensive global conservation of the genomes of these two members of the M. ***tuberculosis*** complex. Possible sites of evolutionary rearrangements were localized on the chromosome of M. bovis BCG Pasteur by comparing the AsnI restriction profile with that of M. ***tuberculosis*** H37Rv. When selected cosmids from the corresponding

areas of the genome of M. ***tuberculosis*** H37Rv were used as hybridization probes to examine different BCG strains, wild-type M. bovis and M. ***tuberculosis*** H37Rv, a number of deletions up to 10 kb in size, insertions and other polymorphisms were detected. In addition to the known deletions covering the genes for the protein antigens ESAT-6 and mpt64, other genetic loci exhibiting polymorphisms or rearrangements were detected in M. bovis BCG Pasteur.

L2 ANSWER 54 OF 73 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 23
AN 1996:508066 BIOSIS
DN PREV199699230422
TI The Mycobacterium ***tuberculosis*** purine biosynthetic pathway: Isolation and characterization of the purC and purL genes.
AU Jackson, Mary (1); Berthet, Francois-Xavier; Otal, Isabel; Rauzier, Jean; Martin, Carlos; ***Gicquel, Brigitte*** ; Guilhot, Christophe
CS (1) Unite Genetique Mycobacterienne, Inst. Pasteur, F-75724 Paris France
SO Microbiology (Reading), (1996) Vol. 142, No. 9, pp. 2439-2447.
ISSN: 1350-0872.
DT Article
LA English
AB Genes from the Mycobacterium ***tuberculosis*** purine biosynthetic pathway were identified using purine auxotrophic mutants of Mycobacterium smegmatis obtained by Tn611 transposon mutagenesis. Two approaches were followed in parallel. The first consisted of the complementation of the M. smegmatis purine auxotrophs using a M. ***tuberculosis*** H37Rv shuttle cosmid library. In the second approach, specific probes corresponding to the regions adjacent to the insertion sites of Tn611 in the M. smegmatis genome were used to screen a M. ***tuberculosis*** plasmid library by colony hybridization for inserts carrying homologous DNA fragments. Nucleotide sequence analysis of two M. ***tuberculosis*** genes isolated by these methods revealed high similarities with purC and purL genes from other bacterial and fungal sources. Transcriptional start sites were mapped for both genes, which revealed similar -10 boxes but with a higher GC content than the Escherichia coli sigma-70 consensus.

L2 ANSWER 55 OF 73 BIOSIS COPYRIGHT 2001 BIOSIS
AN 1996:475250 BIOSIS
DN PREV199699204806
TI European Commission COST/STD initiative: Report of the Expert Panel IX: Vaccines against ***Tuberculosis*** .
AU Harboe, Morten (1); Andersen, Peter; Colston, Michael J.; ***Gicquel,*** *** Brigitte*** ; Hermans, Peter W. M.; Ivanyi, Juraj; Kaufman, Stefan H. E.
CS (1) Inst. Immunol. Rheumatol., Univ. Oslo, Oslo N-0172 Norway
SO Vaccine, (1996) Vol. 14, No. 7, pp. 701-716.
ISSN: 0264-410X.
DT Article
LA English

L2 ANSWER 56 OF 73 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 24
AN 1995:510202 BIOSIS
DN PREV199598515252
TI The urease locus of Mycobacterium ***tuberculosis*** and its utilization for the demonstration of allelic exchange in Mycobacterium bovis bacillus Calmette-Guerin.
AU Reyrat, Jean-Marc (1); Berthet, Francois-Xavier; ***Gicquel, Brigitte***

CS (1) Unite Genet. Mycobacterienne, Cent. Natl. Rech. Sci., Unite Rech. Assoc. 1300, Inst. Pasteur 25, rue du Dr. Roux, F-75724 Paris France

SO Proceedings of the National Academy of Sciences of the United States of America, (1995) Vol. 92, No. 19, pp. 8768-8772.
ISSN: 0027-8424.

DT Article

LA English

AB The ureABC genes of Mycobacterium ***tuberculosis*** were cloned. By using a set of degenerate primers corresponding to a conserved region of the urease enzyme (EC 3.5.1.5), a fragment of the expected size was amplified by PCR and was used to screen a M. ***tuberculosis*** cosmid library. Three open reading frames with extensive similarity to the urease genes from other organisms were found. The locus was mapped on the chromosome, using an ordered M. ***tuberculosis*** cosmid library. A suicide vector containing a ureC gene disrupted by a kanamycin marker (aph) was used to construct a urease-negative Mycobacterium bovis bacillus Calmette-Guerin mutant by allelic exchange involving replacement of the ureC gene with the aph::ureC construct. To our knowledge, allelic exchange has not been reported previously in the slow-growing mycobacteria. Homologous recombination will be an invaluable genetic tool for deciphering the mechanisms of ***tuberculosis*** pathogenesis, a disease that causes 3 times 10-6 deaths a year worldwide.

L2 ANSWER 57 OF 73 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 25

AN 1995:532731 BIOSIS

DN PREV199598547031

TI Characterization of the Mycobacterium ***tuberculosis*** erp gene encoding a potential cell surface protein with repetitive structures.

AU Berthet, Francois-Xavier; Rauzier, Jean; Lim, Eng Mong; Philipp, Wolfgang; ***Gicquel, Brigitte*** ; Portnol, Denis (1)

CS (1) Unite Genet. Mycobacterienne, Inst. Pasteur, 25 rue du Dr. Roux, 75724 Paris Cedex 15 France

SO Microbiology (Reading), (1995) Vol. 141, No. 9, pp. 2123-2130.
ISSN: 1350-0872.

DT Article

LA English

AB Using the phoA gene fusion methodology adapted to mycobacteria, several Mycobacterium ***tuberculosis*** DNA fragments encoding exported proteins were recently identified. In this paper, the molecular cloning, genomic positioning, nucleotide sequence determination and transcriptional start site mapping of a new M. ***tuberculosis*** gene, identified by this methodology, are reported. This gene was called erp (for exported repetitive protein) and has a sequence similar to that of the Mycobacterium leprae 28 kDa antigen irg gene M. ***tuberculosis*** erp gene contains a putative iron box close to the mapped transcriptional start site. The predicted Erp protein displays a typical N-terminal signal sequence, a hydrophobic domain at the C-terminus and harbors repeated amino acid motifs. These structural features are reminiscent of cell-wall-associated surface proteins from Gram-positive bacteria. We found that these repeats are conserved among M. ***tuberculosis*** isolates, and are absent from the published M. leprae irg gene sequence. In addition to being present in M. leprae, erp sequences were found in other members of the M. ***tuberculosis*** complex, but not in other mycobacteria tested. These results suggest that erp might encode a cell surface component shared by major pathogenic mycobacteria.

L2 ANSWER 58 OF 73 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 26
AN 1995:370117 BIOSIS
DN PREV199598384417
TI Chromosomal DNA fingerprinting analysis using the insertion sequence IS6110 and the repetitive element DR as strain-specific markers for epidemiological study of ***tuberculosis*** in French Polynesia.
AU Torrea, Gabriela (1); Levee, Geraldine; Grimont, Patrick; Martin, Carlos; Chanteau, Suzanne; ***Gicquel, Brigitte***
CS (1) Unite Genetique Mycobacterienne, Inst. Pasteur, 25 rue du Dr. Roux, 75724 Paris Cedex 15 France
SO Journal of Clinical Microbiology, (1995) Vol. 33, No. 7, pp. 1899-1904. ISSN: 0095-1137.
DT Article
LA English
AB The polymorphism of Mycobacterium ***tuberculosis*** strains was evaluated in French Polynesia, an area with a low incidence of ***tuberculosis*** and a population which has been geographically stable during recent decades. Nonrepetitive strains isolated from 64 patients during 1991 and 1992 were subjected to DNA restriction fragment length polymorphism (RFLP) analysis, using the insertion sequence IS6110 and the repetitive element DR as probes. Thirty-eight different IS6110 RFLP types were identified. They could be clustered in 11 groups. All the members of each group are identical or differ by one to three bands. All the other strains are gathered in the miscellaneous group. In some cases, transmission of strains with identical RFLP types between patients of the same family or between patients living in the same area was identified. Strains exhibiting similar IS6110 RFLP types also exhibited identical DR RFLP patterns, confirming that strains with similar types were genetically linked. Strains belonging to two different IS6110 clusters exhibited the same DR RFLP type. These data may also indicate a common origin for these strains and evolution to new IS6110 types. The results obtained in this study suggest that not only reactivation of latent tuberculous infections but also active transmissions are still occurring in French Polynesia.

L2 ANSWER 59 OF 73 BIOSIS COPYRIGHT 2001 BIOSIS
AN 1995:367480 BIOSIS
DN PREV199598381780
TI BCG as a vector for the construction of multivalent recombinant vaccines.
AU ***Gicquel, Brigette***
CS Unite de Genetique Mycobacterienne, CNRS URA 1300, Institut Pasteur, 25 rue du Dr. Roux, Paris 75724 Cedex 15 France
SO Biologicals, (1995) Vol. 23, No. 2, pp. 113-118. ISSN: 1045-1056.
DT General Review
LA English

L2 ANSWER 60 OF 73 BIOSIS COPYRIGHT 2001 BIOSIS
AN 1995:147962 BIOSIS
DN PREV199598162262
TI Identification of Mycobacterium ***tuberculosis*** DNA sequences encoding exported proteins, using PhoA gene fusions.
AU Portnoi, Denis; Lim, Eng-Mong; Berthet, Francois-Xavier; Timm, Juliano; ***Gicquel, Brigitte***
CS Unite Genet. Mycobacterienne, CNRS URA 1300, Inst. Pasteur, 75015 Paris

France
SO Journal of Cellular Biochemistry Supplement, (1995) Vol. 0, No. 19B, pp. 78.
Meeting Info.: Keystone Symposium on Molecular Mechanisms in Tuberculosis Tamarron, Colorado, USA February 19-25, 1995
ISSN: 0733-1959.
DT Conference
LA English

L2 ANSWER 61 OF 73 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 27
AN 1995:77452 BIOSIS
DN PREV199598091752
TI Identification of Mycobacterium ***tuberculosis*** DNA Sequences Encoding Exported Proteins by Using phoA Gene Fusions.
AU Lim, Eng Mong; Rauzier, Jean; Timm, Juliano; Torrea, Gabriela; Murray, Alan; ***Gicquel, Brigitte*** ; Portnoi, Denis (1)
CS (1) Unite Genet. Mycobacterienne, CNRS URA 1300, Inst. Pasteur, 25 rue Dr. Roux, 75724 Paris Cedex 15 France
SO Journal of Bacteriology, (1995) Vol. 177, No. 1, pp. 59-65.
ISSN: 0021-9193.
DT Article
LA English
AB The activity of bacterial alkaline phosphatase (PhoA) is dependent on it being exported across the plasma membrane. A plasmid vector (pJEM11) allowing fusions between phoA and genes encoding exported proteins was constructed to study protein export in mycobacteria. Introduction of the Mycobacterium fortuitum beta-lactamase gene (blaF*) into this vector led to the production in M. smegmatis of protein fusions with PhoA activity. A genomic library from M. ***tuberculosis*** was constructed in pJEM11 and screened in M. smegmatis for clones with PhoA activity. Sequences of the M. ***tuberculosis*** inserts directing the production of protein fusions in these PhoA-positive clones were determined. They include part of the already-known exported 19-kDa lipoprotein, a sequence with similarities to the exported 28-kDa antigen from M. leprae, a sequence encoding a protein sharing conserved amino acid motifs with stearoyl-acyl-carrier-protein desaturases, and unknown sequences. This approach thus appears to identify sequences directing protein export, and we expect that more extensive screening of such libraries will lead to a better understanding of protein export in M. ***tuberculosis*** .

L2 ANSWER 62 OF 73 BIOSIS COPYRIGHT 2001 BIOSIS
AN 1994:414711 BIOSIS
DN PREV199497427711
TI Transposition in mycobacteria.
AU McAdam, Ruth A. (1); Guilhot, Christophe; ***Gicquel, Brigitte***
CS (1) Dep. Microbiol. Immunol., Albert Einstein Coll. Med. Yeshiva Univ., 1300 Morris Park Ave., Bronx, NY 10461 USA
SO Bloom, B. R. [Editor]. (1994) pp. 199-216. Tuberculosis: Pathogenesis, protection, and control.
Publisher: American Society for Microbiology (ASM) Books Division, 1325 Massachusetts Ave. NW, Washington, DC 20005-4171, USA.
ISBN: 1-55581-072-1.
DT Book
LA English

L2 ANSWER 63 OF 73 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 28
AN 1994:545368 BIOSIS
DN PREV199598004916
TI Escherichia coli-Mycobacteria Shuttle Vectors for Operon and Gene Fusions to lacZ: The pJEM Series.
AU Timm, Juliano (1); Lim, Eng Mong; ***Gicquel, Brigitte***
CS (1) Unite Genet. Mycobacterienne, CNRS URA 1300, Inst. Pasteur, 25 rue du Dr. Roux, 75015 Paris Cedex 15 France
SO Journal of Bacteriology, (1994) Vol. 176, No. 21, pp. 6749-6753. ISSN: 0021-9193.
DT Article
LA English
AB A series of Escherichia coli-mycobacteria shuttle plasmids for the isolation and study of gene regulatory sequences was constructed. These pJEM vectors contain an efficient transcription terminator and multiple cloning sites and allow either operon or gene fusions to lacZ. By constructing operon fusions with pJEM15, we assessed various previously characterized mycobacterial promoters in the fast-growing species Mycobacterium and the slow-growing species M. bovis BCG. Our results suggest that M. smegmatis and M. bovis BCG RNA polymerases do not share the same specificity. To isolate new mycobacterial promoters, an M. ***tuberculosis*** DNA library was generated, using pJEM13, and screened in M. smegmatis. Several Lac+ clones were isolated, and the beta-galactosidase activity was measured.

L2 ANSWER 64 OF 73 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 29
AN 1994:545335 BIOSIS
DN PREV199598004883
TI Insertion sequence IS1137, a new IS3 family element from Mycobacterium smegmatis.
AU Garcia, Maria J. (1); Guilhot, Christophe; Lathigra, Raju; Menendez, M. Carmen; Domenech, Pilar; Moreno, Carlos; ***Gicquel, Brigitte*** ; Martin, Carlos
CS (1) Dep. Medicina Preventiva, Fac. Medicina, Univ. Autonoma, Arzobispo Morcillo 4, 28029 Madrid Spain
SO Microbiology (Reading), (1994) Vol. 140, No. 10, pp. 2821-2828. ISSN: 1350-0872.
DT Article
LA English
AB A new insertion sequence (IS) has been isolated from Mycobacterium smegmatis. It is 1361 bp long and possesses characteristics of the IS3 family elements. It harbours 32 bp imperfect inverted repeats at its extremities and a 3 bp direct repeat flanks the element, possibly as the result of a transposition event. This IS, IS1137, contains three major ORFs. Two of them, ORF A and ORF B show homologies both at the amino acid sequence level and at the organization level with the ORFs encoding the transposase of the IS3 family elements. IS1137 has a narrow host range and was found only in M. smegmatis and M. chitae. The fact that IS1137 is not present in the M. ***tuberculosis*** complex strains makes this element a new candidate for transposon mutagenesis in mycobacteria.

L2 ANSWER 65 OF 73 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 30
AN 1994:109128 BIOSIS
DN PREV199497122128
TI Efficient transposition in mycobacteria: Construction of Mycobacterium

smegmatis insertional mutant libraries.
AU Guilhot, Christophe (1); Otal, Isabel; Van Rompaey, Ingrid; Martin, Carlos; ***Gicquel, Brigitte***
CS (1) Unite Genet. Mycobacter., URA1300 CNRS, Inst. Pasteur, 25 rue Dr. Roux, F-75015 Paris France
SO Journal of Bacteriology, (1994) Vol. 176, No. 2, pp. 535-539. ISSN: 0021-9193.
DT Article
LA English
AB The Tn611 transposon was inserted into pCG63, a temperature-sensitive plasmid isolated from an Escherichia coli-mycobacterial shuttle vector which contains the pAL5000 and pUC18 replicons. The resulting plasmid, pCG79, was used to generate a large number of insertional mutations in Mycobacterium smegmatis. These are the first mycobacterial insertional mutant libraries to be constructed by transposition directly into a mycobacterium. No highly preferential insertion sites were detected by Southern blot analysis of the chromosomal DNAs isolated from the insertion mutants. Auxotrophic mutants with various phenotypes were isolated at a frequency ranging from 0.1 to 0.4%, suggesting that the libraries are representative. The pCG79 system thus seems to be a useful tool for the study of M. smegmatis genetics and may be applicable to other mycobacteria, such as the M. ***tuberculosis*** complex.

L2 ANSWER 66 OF 73 CAPLUS COPYRIGHT 2001 ACS
AN 1995:645391 CAPLUS
DN 123:133961
TI New methods for diagnosis and epidemiological studies of ***tuberculosis*** based on PCR and RFLP
AU Martin, Carlos; Samper, Sofia; Otal, Isabel; Asensio, Pilar; Gomez-Lus, Rafael; Torrea, Gabriela; ***Gicquel, Brigitte***
CS Facultad de Medicina, Universidad Zaragoza, Spain
SO FEMS Symp. (1994), 75, 105-13
CODEN: FEMSDW; ISSN: 0163-9188
DT Journal; General Review
LA English
AB A review with 33 refs.

L2 ANSWER 67 OF 73 CAPLUS COPYRIGHT 2001 ACS
AN 1993:575418 CAPLUS
DN 119:175418
TI A new promoter from Mycobacterium paratuberculosis and its use in the expression of heterologous genes
IN Murray, Alan; Gheorghiu, Marina; ***Gicquel, Brigitte***
PA Institut Pasteur, Fr.; Massey University
SO Fr. Demande, 69 pp.
CODEN: FRXXBL
DT Patent
LA French
FAN.CNT 2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI FR 2682967	A1	19930430	FR 1991-13227	19911025
FR 2682967	B1	19940114		
EP 666917	A1	19950816	EP 1992-922721	19921023
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, SE				

US 5968815 A 19991019 US 1994-211718 19941006
PRAI FR 1991-13227 19911025
WO 1992-EP2431 19921023

AB A novel promoter, Mptb, from Mycobacterium paratuberculosis is cloned and characterized for use in the expression of heterologous genes in a no. of hosts. The promoter was cloned by screening a genomic bank in .lambda.gt11 by screening for sequences found in M. paratuberculosis but not in M. phlei. The cloned sequence did not hybridize to DNA from M. avium, M. intracellulare, M. ***tuberculosis*** , M. bovis, M. phlei, M. smegmatis or Nocardia asteroides, although it did hybridize to all isolates of M. paratuberculosis tested. The sequence was found to contain two open reading frames and a well-defined promoter region; one of these open reading frames showed some similarity to a sequence from IS900. The use of the promoter to express heterologous genes in M. paratuberculosis and Mycobacterium BCG was demonstrated. The use of the promoter to genes for antigens in Mycobacterium BCG for live vaccines is demonstrated using a reporter gene in mice.

L2 ANSWER 68 OF 73 BIOSIS COPYRIGHT 2001 BIOSIS
AN 1993:438490 BIOSIS
DN PREV199396093115
TI Large-scale DNA fingerprinting of Mycobacterium ***tuberculosis*** strains as a tool for epidemiological studies of ***tuberculosis*** .
AU Chevrel-Dellagi, Denise (1); Abderrahman, Amel; Haltiti, Raja; Koubaji, Hichem; ***Gicquel, Brigitte*** ; Dellagi, Koussay
CS (1) Lab. Mycobacteries, Inst. Pasteur Tunis 13, Place Pasteur, BP 74, 1002 Tunis-Belvedere France
SO Journal of Clinical Microbiology, (1993) Vol. 31, No. 9, pp. 2446-2450. ISSN: 0095-1137.
DT Article
LA English
AB We conducted a large-scale DNA fingerprinting analysis of Mycobacterium ***tuberculosis*** strains in a country in which ***tuberculosis*** is endemic (Tunisia) in order to evaluate the importance of microepidemics in the maintenance of the disease within the population. The genetic polymorphisms of 201 strains of M. ***tuberculosis*** isolated from 196 unrelated patients living in four districts of northern Tunisia during a 3-year period were studied by restriction fragment length polymorphism (RFLP) analysis by using the insertion sequence IS6110 as a probe. Seventy-three strains isolated from 68 patients living in the districts of Tunis, Nabeul, and Jendouba generated 67 different RFLPs, indicating a high degree of polymorphism of the M. ***tuberculosis*** strains within these areas. In contrast, the 128 strains isolated from individuals in the district of Menzel Bourguiba appeared much less heterogeneous since they often generated identical or very similar fingerprints. Seventeen of 29 cases (58%) of active ***tuberculosis*** in the city of Menzel Bourguiba could be traced to as few as four M. ***tuberculosis*** strains. These results indicate the persistence of underestimated microepidemics in this region. The RFLP typing of a large number of randomly collected strains provides a general picture of the strains involved in ***tuberculosis*** . The systematic study of limited areas where ***tuberculosis*** is endemic can provide evidence for the existence of persisting epidemics. This stresses the different problems which remain to be solved in order to improve the control of ***tuberculosis*** .

L2 ANSWER 69 OF 73 BIOSIS COPYRIGHT 2001 BIOSIS
AN 1993:187641 BIOSIS
DN PREV199395098091
TI Strain identification of Mycobacterium ***tuberculosis*** by DNA fingerprinting: Recommendations for a standardized methodology.
AU Van Embden, Jan D. A. (1); Cave, M. Donald; Crawford, Jack T.; Dale, Jeremy W.; Eisenach, Kathleen D.; ***Gicquel, Brigitte*** ; Hermans, Peter; Martin, Carlos; McAdam, Ruth; et al.
CS (1) Unit Mol. Microbiol., Natl. Inst. Public Health Environ. Protection, P.O. Box 1, 3720 BA Bilthoven Netherlands Antilles
SO Journal of Clinical Microbiology, (1993) Vol. 31, No. 2, pp. 406-409. ISSN: 0095-1137.
DT Article
LA English
AB DNA fingerprinting of Mycobacterium ***tuberculosis*** has been shown to be a powerful epidemiologic tool. We propose a standardized technique which exploits variability in both the number and genomic position of IS6110 to generate strain-specific patterns. General use of this technique will permit comparison of results between different laboratories. Such comparisons will facilitate investigations into the international transmission of ***tuberculosis*** and may identify specific strains with unique properties such as high infectivity, virulence, or drug resistance.

L2 ANSWER 70 OF 73 CAPLUS COPYRIGHT 2001 ACS
AN 1991:486777 CAPLUS
DN 115:86777
TI DNA fragments of Mycobacterial genomes for diagnosis of Mycobacteria infections
IN Guesdon, Jean Luc; Thierry, Dominique; Ullmann, Agnes; ***Gicquel,*** *** Brigitte*** ; Brisson-Noel, Anne
PA Institut Pasteur, Fr.
SO PCT Int. Appl., 58 pp.
CODEN: PIXXD2
DT Patent
LA French
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9103558	A1	19910321	WO 1990-FR591	19900906
W: CA, JP, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, IT, LU, NL, SE				
FR 2651505	A1	19910308	FR 1989-11665	19890906
FR 2651505	B1	19940722		
FR 2659086	A1	19910906	FR 1990-2676	19900302
FR 2659086	B1	19920612		
CA 2065424	AA	19910307	CA 1990-2065424	19900906
EP 490951	A1	19920624	EP 1990-913490	19900906
EP 490951	B1	19960424		
R: AT, BE, CH, DE, DK, ES, FR, GB, IT, LI, LU, NL, SE				
JP 05500006	T2	19930114	JP 1990-512609	19900906
AT 137264	E	19960515	AT 1990-913490	19900906
ES 2088432	T3	19960816	ES 1990-913490	19900906
US 5597911	A	19970128	US 1992-829016	19920414

US 5807672 A 19980915 US 1995-487651 19950607
US 5837455 A 19981117 US 1995-487645 19950607
PRAI FR 1989-11665 19890906
FR 1990-2676 19900302
WO 1990-FR591 19900906
US 1992-829016 19920414
AB A DNA sequence which can be used to diagnose Mycobacterium ***tuberculosis*** infection is identified. M. ***tuberculosis*** genomic DNA was cloned and screened with labeled DNA from M. ***tuberculosis*** and M. bovis-BCG. A 1.7 kb fragment which hybridized strongly to the former and weakly to the latter, and which had >50% homol. with insertion sequence IS3411 was identified. Using polymerase chain reaction primers and hybridization probes derived from this sequence, .apprx.10 fg M. tuberculisis DNA (corresponding to .apprx.3 bacteria) was detectable in <24 h. M. ***tuberculosis*** was also detected in clin. samples using such hybridization assays.

L2 ANSWER 71 OF 73 CAPLUS COPYRIGHT 2001 ACS
AN 1991:552048 CAPLUS
DN 115:152048
TI Restriction fragment length polymorphism analysis using IS6110 as an epidemiological marker in ***tuberculosis***
AU Otal, Isabel; Martin, Carlos; Vincent-Levy-Frebault, Veronique; Thierry, Dominique; ***Gicquel, Brigitte***
CS Unite Gen. Microbiol., Inst. Pasteur, Paris, 75015, Fr.
SO J. Clin. Microbiol. (1991), 29(6), 1252-4
CODEN: JCMIDW; ISSN: 0095-1137
DT Journal
LA English
AB The mycobacterial insertion sequence IS6110 has been shown to be present in multiple copies in the chromosome of Mycobacterium ***tuberculosis*** . IS6110 restriction fragment length polymorphism anal. of strains isolated from patients who developed ***tuberculosis*** showed identical patterns over a 2- to 3-yr period. In contrast, a high degree of polymorphism was obsd. between strains of the M. ***tuberculosis*** complex isolated from different patients. This study demonstrates that the presence of IS6110 does not induce in vivo major genomic rearrangements over a 2- to 3-yr period and confirms its use as a valuable epidemiol. marker in ***tuberculosis*** .

L2 ANSWER 72 OF 73 CAPLUS COPYRIGHT 2001 ACS
AN 1991:443531 CAPLUS
DN 115:43531
TI Nucleotide primer and probe sequences of Actinomycetales, applications to the synthesis or detection of nucleic acids, products of expression of such sequences, and application as immunogenic compositions
IN Hance, Allan Johnson; Grandchamp-Desraux, Bernard; Levy-Frebault, Veronique; ***Gicquel, Brigitte***
PA Institut National de la Sante et de la Recherche Medicale (INSERM), Fr.; Institute Pasteur
SO PCT Int. Appl., 65 pp.
CODEN: PIXXD2
DT Patent
LA French
FAN.CNT 1

PATENT NO. KIND DATE APPLICATION NO. DATE

PI WO 9012875 A1 19901101 WO 1990-FR274 19900413
W: CA, JP, US
RW: AT, BE, CH, DE, DK, ES, FR, GB, IT, LU, NL, SE
FR 2645878 A1 19901019 FR 1989-5057 19890417
FR 2645878 B1 19940225
CA 2031195 AA 19901018 CA 1990-2031195 19900413
EP 419648 A1 19910403 EP 1990-907137 19900413
R: AT, BE, CH, DE, DK, ES, FR, GB, IT, LI, LU, NL, SE
JP 03505974 T2 19911226 JP 1990-506961 19900413
US 5817459 A 19981006 US 1991-623729 19910211
US 5877273 A 19990302 US 1995-473020 19950606
PRAI FR 1989-5057 19890417
WO 1990-FR274 19900413
US 1991-623729 19910211
OS MARPAT 115:43531
AB Nucleotide sequences, and fragments thereof, of Actinomycetales, esp. Mycobacteria, are provided as DNA synthesis primers and as probes for detection of DNA and/or transcription products of Actinomycetales. Also provided are the peptide products coded by the nucleotide sequences, antibodies to the peptides, and immunogenic compns. comprising the peptides. The Actinomycetales nucleotide sequence comprises a homologous sequence of a gene common to all Actinomycetales, within which exist conserved and variable regions. Sequences of the nucleotides and peptides of the invention are given. Using the methods of the invention, it was possible to detect e.g. .apprx.10 BCG/mL pleural fluid.

L2 ANSWER 73 OF 73 CAPLUS COPYRIGHT 2001 ACS
AN 1991:404376 CAPLUS
DN 115:4376
TI Characterization of a Mycobacterium ***tuberculosis*** insertion sequence, IS6110, and its application in diagnosis
AU Thierry, Dominique; Brisson-Noel, Anne; Vincent-Levy-Frebault, Veronique; Nguyen, Simon; Guesdon, Jean Luc; ***Gicquel, Brigitte***
CS Lab. Sondes Froides, Inst. Pasteur, Paris, 75015, Fr.
SO J. Clin. Microbiol. (1990), 28(12), 2668-73
CODEN: JCMIDW; ISSN: 0095-1137
DT Journal
LA English
AB An insertion sequence-like element, IS6001, was isolated from a M. ***tuberculosis*** cosmid library as a repetitive sequence. IS6110 shows similarities with elements of the IS3 family. This insertion sequence was found to be specific to mycobacteria belonging to the M. ***tuberculosis*** complex. For detection and identification of M. ***tuberculosis*** bacilli in uncultured specimens, oligonucleotides derived from the IS6110 sequence were used as primers and probes in polymerase chain reaction studies. The results obtained were consistent with results of classical identification procedures, bacteriol. data, and clin. criteria.

=> e berthet francois/au
E1 2 BERTHET FLORENTIN/AU
E2 2 BERTHET FRANCK/AU

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E3        0 --> BERTHET FRANCOIS/AU
E4       20    BERTHET FRANCOIS XAVIER/AU
E5        1    BERTHET FRANCOIS XAVIER JACQUES/AU
E6        3    BERTHET FRANCOISE/AU
E7        2    BERTHET FREDERIC/AU
E8       57    BERTHET G/AU
E9       15    BERTHET GINETTE/AU
E10       2    BERTHET GWENAEL/AU
E11      15    BERTHET H/AU
E12       4    BERTHET HUBERT/AU

=> s e3-e6
L3       24 ("BERTHET FRANCOIS"/AU OR "BERTHET FRANCOIS XAVIER"/AU OR "BERTH
           ET FRANCOIS XAVIER JACQUES"/AU OR "BERTHET FRANCOISE"/AU)

=> dup rem l3
PROCESSING COMPLETED FOR L3
L4       16 DUP REM L3 (8 DUPLICATES REMOVED)

=> d bib ab 1-
YOU HAVE REQUESTED DATA FROM 16 ANSWERS - CONTINUE? Y/(N):y


L4  ANSWER 1 OF 16  CAPLUS  COPYRIGHT 2001 ACS
AN  2001:101328  CAPLUS
DN  134:146387
TI  Immuno-protective and non-toxic Gram-neg. bleb vaccine suitable for
    pediatric use
IN  ***Berthet, Francois-xavier Jacques***  ; Dalemans, Wilfried L. J.;
    Denoel, Philippe; Dequesne, Guy; Feron, Christiane; Lobet, Yves; Poolman,
    Jan; Thiry, Georges; Thonnard, Joelle; Voet, Pierre
PA  Smithkline Beecham Biologicals S.A., Belg.
SO  PCT Int. Appl., 128 pp.
    CODEN: PIXXD2
DT  Patent
LA  English
FAN.CNT 1
    PATENT NO.      KIND  DATE        APPLICATION NO.  DATE
    --------------- ----  --------    ---------------  --------
PI  WO 2001009350   A2    20010208    WO 2000-EP7424   20000731
        W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
           CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR,
           HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT,
           LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU,
           SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN,
           YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
        RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
           DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ,
           CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
PRAI GB 1999-18319    A   19990803
AB  The present invention relates to an immuno-protective and non-toxic
    Gram-neg. bleb vaccine suitable for pediatric use. Examples of the
    Gram-neg. strains from which the blebs are made are N. meningitidis, M.
    catarrhalis and H. influenzae. The blebs of the invention are improved by
    one or more genetic changes to the chromosome of the bacterium, including
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up-regulation of protective antigens, down-regulation of immunodominant non-protective antigens, and detoxification of the Lipid A moiety of LPS.

L4 ANSWER 2 OF 16 USPATFULL
AN 2001:93348 USPATFULL
TI Mycobacteria functional screening and/or expression vectors
IN Gicquel, Brigitte, Paris, France
Lim, Eng Mong, Paris, France
Portnoi, Denis, Paris, France
Berthet, Francois-Xavier , Paris, France
Timm, Juliano, Paris, France
PA Institut Pasteur, Paris Cedex, France (non-U.S. corporation)
PI US 6248581 B1 20010619
WO 9607745 19960314
AI US 1997-793701 19970609 (8)
WO 1995-FR1133 19950830
19970609 PCT 371 date
19970609 PCT 102(e) date
PRAI FR 1994-104585 19940902
DT Utility
EXNAM Primary Examiner: Swartz, Rodney P.
LREP Finnegan, Henderson, Farabow, Garrett & Dunner, L.L.P.
CLMN Number of Claims: 21
ECL Exemplary Claim: 1
DRWN 19 Drawing Figure(s); 18 Drawing Page(s)
LN.CNT 1360
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Recombinant screening, cloning and/or expression vector characterized in that it replicates in mycobacteria and contains 1) a mycobacteria functional replicon; 2) a selection marker, 3) a reporter cassette comprising a) a multiple cloning site (polylinker) b) a transcription terminator which is active in mycobacteria and is located upstream of the polylinker, and c) a coding nucleotide sequence derived from a gene coding for an expression, export and/or secretion protein marker, the nucleotide sequence being deprived of its initiation codon and its regulating sequences. This vector is used for identification and expression of exporter polypeptides, such as the Mycobacterium tuberculosis P28 antigen.

L4 ANSWER 3 OF 16 CAPLUS COPYRIGHT 2001 ACS
AN 1999:96265 CAPLUS
DN 130:165435
TI Mycobacterium strain with modified erp gene and vaccine composition containing the same
IN Gicquel, Brigitte; ***Berthet, Francois-Xavier***
PA Institut Pasteur, Fr.
SO PCT Int. Appl., 53 pp.
CODEN: PIXXD2
DT Patent
LA French
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9905168	A1	19990204	WO 1998-FR1627	19980722

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE,

DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG,
KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX,
NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT,
UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES,
FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI,
CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
FR 2766495 A1 19990129 FR 1997-9303 19970722
AU 9888671 A1 19990216 AU 1998-88671 19980722
EP 991663 A1 20000412 EP 1998-940318 19980722
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, FI
PRAI FR 1997-9303 19970722
WO 1998-FR1627 19980722
AB The invention concerns Mycobacterium strains whereof the erp gene is modified and a vaccine compn. contg. same. The modification of the erp gene decreases the virulence and the persistence of the Mycobacterium strains.
RE.CNT 6
RE
(1) Berthet, F; Microbiology 1995, V141(9), P2123 CAPLUS
(2) Lim, E; Journal of Bacteriology 1995, V177(1), P59 CAPLUS
(3) Pasteur Institut; WO 9607745 A 1996 CAPLUS
(4) Pasteur Institut; WO 9623885 A 1996 CAPLUS
(5) Pelicic, V; FEMS Microbiology Letters 1996, V144, P161 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 4 OF 16 CAPLUS COPYRIGHT 2001 ACS
AN 1999:77692 CAPLUS
DN 130:165432
TI The antigenic protein LHP of Mycobacterium tuberculosis and the lhp gene encoding it and their diagnostic and prophylactic uses
IN Gicquel, Brigitte; ***Berthet, Francois-Xavier*** ; Andersen, Peter; Rasmussen, Peter Birk
PA Institut Pasteur, Fr.; Statens Serum Institut
SO PCT Int. Appl., 88 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9904005	A1	19990128	WO 1998-IB1091	19980716

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

AU 9881238	A1	19990210	AU 1998-81238	19980716
EP 1003870	A1	20000531	EP 1998-930967	19980716

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI

PRAI US 1997-52631 P 19970716
WO 1998-IB1091 W 19980716

AB The Mycobacterium tuberculosis gene encoding the antigenic protein LHP that is homologous to the L45 antigen of M. bovis, is cloned and characterized. The gene can be expressed from its own promoter in slow-growing (M. tuberculosis group) and fast-growing (M. smegmatis) mycobacteria. The LHP gene product, and antigenic peptides derived from it, can be manufd. for use in vaccines and to raise reagent antibodies for diagnostic use. The promoter of the lhp gene may be of use in the expression of foreign genes in Mycobacteria. Oligonucleotides derived from the promoter region may be useful as probes or primers in the detection of M. tuberculosis in a biol. sample. Anal. of the promoters driving expression of the closely linked lhp and orf1C genes of M. tuberculosis established that they form an operon. Use of the promoter to drive expression of a reporter gene in M. smegmatis is demonstrated. The protein is abundant in short-term (7 day) culture filtrates of M. tuberculosis.

RE.CNT 9

RE

(1) Ajinomoto Kk; EP 0400973 A 1990 CAPLUS
(3) Corixa Corp; WO 9709428 A 1997 CAPLUS
(4) Corixa Corp; WO 9709429 A 1997 CAPLUS
(5) Corixa Corp; WO 9816645 A 1998 CAPLUS
(6) Corixa Corp; WO 9816646 A 1998 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 5 OF 16 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 1

AN 1999:527380 BIOSIS

DN PREV199900527380

TI Use of fluorescence induction and sucrose counterselection to identify Mycobacterium tuberculosis genes expressed within host cells.

AU Triccas, James A.; ***Berthet, Francois-Xavier*** ; Pelicic, Vladimir; Gicquel, Brigitte (1)

CS (1) Unite de Genetique Mycobacterienne, Institut Pasteur, 25 rue du Dr Roux, 75724, Paris Cedex 15 France

SO Microbiology (Reading), (Oct., 1999) Vol. 145, No. 10, pp. 2923-2930. ISSN: 1350-0872.

DT Article

LA English

SL English

AB The identification of Mycobacterium tuberculosis genes expressed within host cells would contribute greatly to the development of new strategies to combat tuberculosis. By combining the natural fluorescence of the Aequoria victoria green fluorescent protein (GFP) with the counterselectable property of the Bacillus subtilis SacB protein, M. tuberculosis promoters displaying enhanced in vivo activity have been isolated. Macrophages were infected with recombinant Mycobacterium bovis bacille Calmette-Guerin containing a library of M. tuberculosis promoters controlling gfp and sacB expression, and fluorescent bacteria recovered by fluorescence-activated cell sorting. The expression of sacB was used to eliminate clones with strong promoter activity outside the macrophage, resulting in the isolation of seven clones containing M. tuberculosis promoters with greater activity intracellularly. The gene products identified displayed similarity to proteins from other organisms whose functions include nutrient utilization, protection from oxidative stress

and defence against xenobiotics. These proposed functions are consistent with conditions encountered within the host cell and thus suggest that the augmented activity of the isolated promoters/genes may represent strategies employed by M. tuberculosis to enhance intracellular survival and promote infection.

L4 ANSWER 6 OF 16 CAPLUS COPYRIGHT 2001 ACS
AN 1998:753589 CAPLUS
DN 130:120272
TI A Mycobacterium tuberculosis operon encoding ESAT-6 and a novel low-molecular-mass culture filtrate protein (CFP-10)
AU ***Berthet, Francois-Xavier*** ; Rasmussen, Peter Birk; Rosenkrands, Ida; Andersen, Peter; Gicquel, Brigitte
CS Unite de Genetique Mycobacterienne, Institut Pasteur, Paris, 75724, Fr.
SO Microbiology (Reading, U. K.) (1998), 144(11), 3195-3203
CODEN: MROBEO; ISSN: 1350-0872
PB Society for General Microbiology
DT Journal
LA English
AB The early secreted antigenic target 6 kDa protein (ESAT-6) is a potent T-cell protein antigen synthesized by Mycobacterium tuberculosis. Its corresponding gene (esat-6) is located in RD1, a 10kb DNA region deleted in the attenuated tuberculosis vaccine strain Mycobacterium bovis BCG. The promoter region of M. tuberculosis esat-6 was cloned and characterized. A new gene, designated lhp and cotranscribed with esat-6, was identified. Moreover, computer searches in the M. tuberculosis genome identified 13 genes related to the lhp/esat-6 operon, defining a novel gene family. The transcription initiation sites of the lhp/esat-6 operon were mapped using M. tuberculosis RNA. The corresponding promoter signals were not recognized in Mycobacterium smegmatis, in which transcription of lhp/esat-6 is initiated at different locations. The M. tuberculosis lhp gene product was identified as CFP-10, a low-mol.-mass protein found in the short-term culture filtrate. These results show that the genes encoding CFP-10 and ESAT-6 are transcribed together in M. tuberculosis and that both code for small exported proteins.
RE.CNT 22
RE
(1) Andersen, P; Infect Immun 1991, V59, P1558 CAPLUS
(2) Andersen, P; J Immunol 1995, V154, P3359 CAPLUS
(3) Bashyam, M; Biotechniques 1994, V17, P834 CAPLUS
(4) Bashyam, M; J Bacteriol 1996, V178, P4847 CAPLUS
(5) Berthet, F; Microbiology 1995, V141, P2123 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 7 OF 16 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 2
AN 1999:8627 BIOSIS
DN PREV199900008627
TI Attenuation of virulence by disruption of the Mycobacterium tuberculosis erp gene.
AU ***Berthet, Francois-Xavier (1)*** ; Lagranderie, Micheline; Gounon, Pierre; Laurent-Winter, Christine; Ensergueix, Danielle; Chavarot, Pierre; Thouron, Francoise; Maranghi, Eddie; Pelicic, Vladimir; Portnoi, Denis; Marchal, Gilles; Gicquel, Brigitte
CS (1) Unite de Genetique Mycobacterienne, Institut Pasteur, 25 rue du Docteur Roux, 75724 Paris Cedex 15 France

SO Science (Washington D C), (Oct. 23, 1998) Vol. 282, No. 5389, pp. 759-762.
ISSN: 0036-8075.
DT Article
LA English
AB The virulence of the mycobacteria that cause tuberculosis depends on their ability to multiply in mammalian hosts. Disruption of the bacterial erp gene, which encodes the exported repetitive protein, impaired multiplication of M. tuberculosis and M. bovis Bacille Calmette-Guerin in cultured macrophages and mice. Reintroduction of erp into the mutants restored their ability to multiply. These results indicate that erp contributes to the virulence of M. tuberculosis.

L4 ANSWER 8 OF 16 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 3
AN 1998:167737 BIOSIS
DN PREV199800167737
TI Immunosorbent assay based on recombinant hemagglutinin protein produced in a high-efficiency mammalian expression system for surveillance of measles immunity.
AU Bouche, Fabienne; Ammerlaan, Wim; ***Berthet, Francoise*** ; Houard, Sophie; Schneider, Francois; Muller, Claude P. (1)
CS (1) Dep. Immunol., Lab. Natl. Sante, 20A rue Auguste Lumiere, L-1011 Luxembourg Luxembourg
SO Journal of Clinical Microbiology, (March, 1998) Vol. 36, No. 3, pp. 721-726.
ISSN: 0095-1137.
DT Article
LA English
AB Recombinant hemagglutinin (H) protein of the measles virus (NM was produced in mammalian cells with a high-yield expression system based on the Semliki Forest virus replicon. Crude membrane preparations of H protein-transfected BHK-21 cells were used to coat microtiter plates to measure specific immunoglobulin G antibodies in 228 serologically defined serum samples mainly from measles late-convalescent adults. The titers by the enzyme-linked immunosorbent assay for the H protein (H-ELISA) closely correlated with neutralization test (NT) titers (R2 = 0.66), hemagglutination inhibition test (HI) titers (R2 = 0.64), with the titers from a certified commercial ELISA based on whole NW-infected cells (MV-ELISA; R2= 0.45). The correlations described above were better than those of the commercial MV-ELISA titers with the NT (R2 = 0.52) or HI (R2 = 0.48) titers. By using the 2nd International Standard for anti-measles serum, the detection level of the assay corresponds to 215 mIU/ml for undiluted serum, which corresponds to the estimated threshold for protective immunity. The specificity, accuracy, and positive predictive value were, in general, better for the H-ELISA than for a commercial MV-ELISA, independent of whether HI, NT, or HI and NT were used as "gold standards." In contrast, the H-ELISA proved to be slightly less sensitive than the MV-ELISA (sensitivities, 98.6 versus 99.5%, respectively; P was not significant). The assays did not differ significantly in the number of serum samples with positive HI and NT results (n = 212) which measured false negative (H-ELISA, 2 of 212 (0.94%); MV-ELISA, 1 of 212 (0.47%)), but the H-ELISA detected significantly more measles-susceptible individuals than the MV-ELISA (10 of 11 versus 3 of 11, respectively; P < 0.05) among the individuals whose sera had negative HI and NT results. Our data demonstrate that the H-protein preparation that we describe could be a cost-effective alternative to current whole-virus-based ELISAs for

surveillance for immunity to measles and that such an assay could be more efficient in detecting susceptibility to measles. Furthermore, unlike whole MV-based antigens, H-protein would also be suitable for use in the development of a simple field test for the diagnosis of measles.

L4 ANSWER 9 OF 16 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 4
AN 1997:438356 BIOSIS
DN PREV199799737559
TI Extensive nucleotide changes and deletions within the envelope glycoprotein gene of Euro-African West Nile viruses.
AU ***Berthet, Francois-Xavier*** ; Zeller, Herve G.; Drouet, Marie-Therese; Rauzier, Jean; Digoutte, Jean-Pierre; Deubel, Vincent (1)
CS (1) Unite Arbovirus Virus Fievres Hemorragiques, Inst. Pasteur-Paris, 25 rue du Dr. Roux, 75724 Paris Cedex 15 France
SO Journal of General Virology, (1997) Vol. 78, No. 9, pp. 2293-2297. ISSN: 0022-1317.
DT Article
LA English
AB We compared the sequence of an envelope protein gene fragment from 21 temporally distinct West Nile (WN) virus strains, isolated in nine African countries and in France. Alignment of nucleotide sequences defined two groups of viruses which diverged by up to 29%. The first group of subtypes is composed of nine WN strains from France and Africa. The Austral-Asian Kunjin virus was classified as a WN subtype in this first group. The second group includes 12 WN strains from Africa and Madagascar. Four strains harbored a 12 nucleotide in-frame deletion. The loss of the corresponding four amino acids resulted in the loss of the potential glycosylation site present in several WN strains. The distribution of virus subtypes into two lineages did not correlate with host preference or geographical origin. The isolation of closely related subtypes in distant countries is consistent with WN viruses being disseminated by migrating birds.

L4 ANSWER 10 OF 16 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 5
AN 1997:295187 BIOSIS
DN PREV199799594390
TI Aminoglycoside 2'-N-acetyltransferase genes are universally present in mycobacteria: Characterization of the aac(2')-Ic gene from Mycobacterium tuberculosis and the aac(2')-Id gene Mycobacterium smegmatis.
AU Ainsa, Jose A. (1); Perez, Esther; Pelicic, Vladimir; ***Berthet,*** *** Francois-Xavier*** ; Gicquel, Brigitte; Martin, Carlos
CS (1) Dep. Microbiol. Med. Preventiva Salud Publica, Fac. Med., Univ. Zaragoza, 50009-Zaragoza Spain
SO Molecular Microbiology, (1997) Vol. 24, No. 2, pp. 431-441. ISSN: 0950-382X.
DT Article
LA English
AB The genus Mycobacterium comprises clinically important pathogens such as M. tuberculosis, which has reemerged as a major cause of morbidity and mortality world-wide especially with the emergence of multi-drug-resistant strains. The use of fast-growing species such as Mycobacterium smegmatis has allowed important advances to be made in the field of mycobacterial genetics and in the study of the mechanisms of resistance in mycobacteria. The isolation of an aminoglycoside-resistance gene from Mycobacterium fortuitum has recently been described. The aac(2')-Ib gene is

chromosomally encoded and is present in all isolates of M. fortuitum. The presence of this gene in other mycobacterial species is studied here and genes homologous to that of M. fortuitum have been found in all mycobacterial species studied. In this report, the cloning of the aac(2')-Ic gene from M. tuberculosis H37Rv and the aac(2')-Id gene from M. smegmatis mc-2155 is described. Southern blot hybridizations have shown that both genes are present in all strains of this species studied to date. In addition, the putative aac(2')-Ie gene has been located in a recent release of the Mycobacterium leprae genome. The expression of the aac(2')-Ic and aac(2')-Id genes has been studied in M. smegmatis and only aac(2')-Id is correlated with aminoglycoside resistance. In order to elucidate the role of the aminoglycoside 2'-N-acetyltransferase genes in mycobacteria and to determine whether they are silent resistance genes or whether they have a secondary role in mycobacterial metabolism, the aac(2')-Id gene from M. smegmatis has been disrupted in the chromosome of M. smegmatis mc-2155. The disruptant shows an increase in aminoglycoside susceptibility along with a slight increase in the susceptibility to lysozyme.

L4 ANSWER 11 OF 16 CAPLUS COPYRIGHT 2001 ACS
AN 1996:350332 CAPLUS
DN 125:27682
TI Cloning and expression vectors for mycobacterial hosts for detection of genes for secreted proteins
IN Gicquel, Brigitte; Lim, Eng Mong; Portnoi, Denis; ***Berthet,*** *** Francois-Xavier*** ; Timm, Juliano
PA Institut Pasteur, Fr.
SO PCT Int. Appl., 69 pp.
CODEN: PIXXD2
DT Patent
LA French
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9607745	A2	19960314	WO 1995-FR1133	19950830
W: CA, JP, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
FR 2724183	A1	19960308	FR 1994-10585	19940902
FR 2724183	B1	19970411		
CA 2197717	AA	19960314	CA 1995-2197717	19950830
EP 770138	A2	19970502	EP 1995-929147	19950830
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 10504966	T2	19980519	JP 1995-509250	19950830
US 6248581	B1	20010619	US 1997-793701	19970609
PRAI FR 1994-10585	A	19940902		
WO 1995-FR1133	W	19950830		

AB Cloning and expression vectors for identification of genes for secreted proteins of Mycobacteria have a replicon functional in a mycobacterium; a selectable marker; an expression cassette with a multiple cloning site and a transcription terminator. The expression cassette also has a sequence encoding a reporter moiety that lacks a promoter or signal sequence. When a gene for a secreted protein is cloned upstream of the reporter moiety, the distribution of the reporter activity can be used to identify membrane-bound or assocd. or secreted proteins. This vector is used for identification and expression of exported polypeptides, such as the

Mycobacterium tuberculosis P28 antigen for use in new vaccines against Mycobacteria. The use of the vectors is demonstrated by reconstruction expts. using the regulatory and signal regions of the blaF* gene of M. fortuitum to direct secretory expression of an alk. phosphatase (phoA) gene. The same construct was used to identify a no. of genes for secreted proteins of M. tuberculosis.

L4 ANSWER 12 OF 16 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 6
AN 1996:508066 BIOSIS
DN PREV199699230422
TI The Mycobacterium tuberculosis purine biosynthetic pathway: Isolation and characterization of the purC and purL genes.
AU Jackson, Mary (1); ***Berthet, Francois-Xavier*** ; Otal, Isabel; Rauzier, Jean; Martin, Carlos; Gicquel, Brigitte; Guilhot, Christophe
CS (1) Unite Genetique Mycobacterienne, Inst. Pasteur, F-75724 Paris France
SO Microbiology (Reading), (1996) Vol. 142, No. 9, pp. 2439-2447.
ISSN: 1350-0872.
DT Article
LA English
AB Genes from the Mycobacterium tuberculosis purine biosynthetic pathway were identified using purine auxotrophic mutants of Mycobacterium smegmatis obtained by Tn611 transposon mutagenesis. Two approaches were followed in parallel. The first consisted of the complementation of the M. smegmatis purine auxotrophs using a M. tuberculosis H37Rv shuttle cosmid library. In the second approach, specific probes corresponding to the regions adjacent to the insertion sites of Tn611 in the M. smegmatis genome were used to screen a M. tuberculosis plasmid library by colony hybridization for inserts carrying homologous DNA fragments. Nucleotide sequence analysis of two M. tuberculosis genes isolated by these methods revealed high similarities with purC and purL genes from other bacterial and fungal sources. Transcriptional start sites were mapped for both genes, which revealed similar -10 boxes but with a higher GC content than the Escherichia coli sigma-70 consensus.

L4 ANSWER 13 OF 16 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 7
AN 1995:510202 BIOSIS
DN PREV199598515252
TI The urease locus of Mycobacterium tuberculosis and its utilization for the demonstration of allelic exchange in Mycobacterium bovis bacillus Calmette-Guerin.
AU Reyrat, Jean-Marc (1); ***Berthet, Francois-Xavier*** ; Gicquel, Brigitte
CS (1) Unite Genet. Mycobacterienne, Cent. Natl. Rech. Sci., Unite Rech. Assoc. 1300, Inst. Pasteur 25, rue du Dr. Roux, F-75724 Paris France
SO Proceedings of the National Academy of Sciences of the United States of America, (1995) Vol. 92, No. 19, pp. 8768-8772.
ISSN: 0027-8424.
DT Article
LA English
AB The ureABC genes of Mycobacterium tuberculosis were cloned. By using a set of degenerate primers corresponding to a conserved region of the urease enzyme (EC 3.5.1.5), a fragment of the expected size was amplified by PCR and was used to screen a M. tuberculosis cosmid library. Three open reading frames with extensive similarity to the urease genes from other organisms were found. The locus was mapped on the chromosome, using an

ordered M. tuberculosis cosmid library. A suicide vector containing a ureC gene disrupted by a kanamycin marker (aph) was used to construct a urease-negative Mycobacterium bovis bacillus Calmette-Guerin mutant by allelic exchange involving replacement of the ureC gene with the aph::ureC construct. To our knowledge, allelic exchange has not been reported previously in the slow-growing mycobacteria. Homologous recombination will be an invaluable genetic tool for deciphering the mechanisms of tuberculosis pathogenesis, a disease that causes 3 times 10-6 deaths a year worldwide.

L4 ANSWER 14 OF 16 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 8
AN 1995:532731 BIOSIS
DN PREV199598547031
TI Characterization of the Mycobacterium tuberculosis erp gene encoding a potential cell surface protein with repetitive structures.
AU ***Berthet, Francois-Xavier*** ; Rauzier, Jean; Lim, Eng Mong; Philipp, Wolfgang; Gicquel, Brigitte; Portnol, Denis (1)
CS (1) Unite Genet. Mycobacterienne, Inst. Pasteur, 25 rue du Dr. Roux, 75724 Paris Cedex 15 France
SO Microbiology (Reading), (1995) Vol. 141, No. 9, pp. 2123-2130. ISSN: 1350-0872.
DT Article
LA English
AB Using the phoA gene fusion methodology adapted to mycobacteria, several Mycobacterium tuberculosis DNA fragments encoding exported proteins were recently identified. In this paper, the molecular cloning, genomic positioning, nucleotide sequence determination and transcriptional start site mapping of a new M. tuberculosis gene, identified by this methodology, are reported. This gene was called erp (for exported repetitive protein) and has a sequence similar to that of the Mycobacterium leprae 28 kDa antigen irg gene M. tuberculosis erp gene contains a putative iron box close to the mapped transcriptional start site. The predicted Erp protein displays a typical N-terminal signal sequence, a hydrophobic domain at the C-terminus and harbors repeated amino acid motifs. These structural features are reminiscent of cell-wall-associated surface proteins from Gram-positive bacteria. We found that these repeats are conserved among M. tuberculosis isolates, and are absent from the published M. leprae irg gene sequence. In addition to being present in M. leprae, erp sequences were found in other members of the M. tuberculosis complex, but not in other mycobacteria tested. These results suggest that erp might encode a cell surface component shared by major pathogenic mycobacteria.

L4 ANSWER 15 OF 16 BIOSIS COPYRIGHT 2001 BIOSIS
AN 1995:147962 BIOSIS
DN PREV199598162262
TI Identification of Mycobacterium tuberculosis DNA sequences encoding exported proteins, using PhoA gene fusions.
AU Portnoi, Denis; Lim, Eng-Mong; ***Berthet, Francois-Xavier*** ; Timm, Juliano; Gicquel, Brigitte
CS Unite Genet. Mycobacterienne, CNRS URA 1300, Inst. Pasteur, 75015 Paris France
SO Journal of Cellular Biochemistry Supplement, (1995) Vol. 0, No. 19B, pp. 78.
Meeting Info.: Keystone Symposium on Molecular Mechanisms in Tuberculosis

Tamarron, Colorado, USA February 19-25, 1995
ISSN: 0733-1959.
DT Conference
LA English

L4 ANSWER 16 OF 16 BIOSIS COPYRIGHT 2001 BIOSIS
AN 1994:127916 BIOSIS
DN PREV199497140916
TI Clinical consequences and treatment of primary immunodeficiency syndromes characterized by functional T and B lymphocyte anomalies (combined immune deficiency.
AU ***Berthet, Francoise*** ; Le Deist, Francoise; Duliege, Anne Marie; Griscelli, Claude; Fischer, Alan (1)
CS (1) INSERM U 132, Hopital Necker-Enfants Malades, 149 rue de Sevres, 75743 Paris, Cedex 15 France
SO Pediatrics, (1994) Vol. 93, No. 2, pp. 265-270.
ISSN: 0031-4005.
DT Article
LA English
AB Objective. To review the clinical presentation and outcome of patients with an unusual primary T + B lymphocyte immunodeficiency syndrome, characterized by the presence of T lymphocytes with no detectable gross phenotypic anomaly, but which are not activated in vitro or in vivo in response to antigens, although they do respond to mitogens. Methods. A retrospective analysis of clinical and immunological data recorded in 25 cases. Acquired immunodeficiencies and known primary T cell immunodeficiency syndromes (severe combined immunodeficiency syndrome, Di-George syndrome, Wiskott-Aldrich syndrome, cartilage hair hypoplasia, Omenn's syndrome, ataxia telangiectasia, defective expression of major histocompatibility complex class 11 molecules, and defective expression of the CD3/T cell receptor complex) were excluded. Results. The patients had severe and particularly protracted infections, mainly of the respiratory tract and gut. Severe viral infections, generally due to herpes viruses, occurred in nearly two-thirds of the patients, with a median follow-up of 54 months. Autoimmune manifestations are frequent (60%), targetting mainly marrow-derived cells, and were characterized by a tendency to relapse and by a dependence on immunosuppressive therapy. Allergic manifestations were also frequent (48% of cases). Eight of the 19 patients who had not undergone bone marrow transplantation died. All but one of the 11 survivors had moderate to severe sequelae. Bone marrow transplantation seemed to be the treatment of choice, because four of six recipients of HLA-identical (n = 2) or nonidentical (n = 4) marrow are alive and the immune deficiency has been corrected. Conclusion. Early recognition of these life-threatening syndromes may improve the chances of cure. Despite common clinical manifestations and prognosis, these functional immunodeficiencies appear heterogeneous regarding inheritance pattern and at least existence of a B cell immunodeficiency.

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E2 1 ANDERSEN PETE/AU
E3 152 --> ANDERSEN PETER/AU
E4 1 ANDERSEN PETER A/AU
E5 2 ANDERSEN PETER B/AU

E6 37 ANDERSEN PETER C/AU
E7 19 ANDERSEN PETER E/AU
E8 4 ANDERSEN PETER F/AU
E9 71 ANDERSEN PETER H/AU
E10 4 ANDERSEN PETER HOENGAARD/AU
E11 12 ANDERSEN PETER HONGAARD/AU
E12 1 ANDERSEN PETER HUNDEVADT/AU

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L6 61 DUP REM L5 (36 DUPLICATES REMOVED)

=> d bib ab 1-
YOU HAVE REQUESTED DATA FROM 61 ANSWERS - CONTINUE? Y/(N):y

L6 ANSWER 1 OF 61 BIOSIS COPYRIGHT 2001 BIOSIS
AN 2001:94979 BIOSIS
DN PREV200100094979
TI Use of ESAT-6 and CFP-10 antigens for diagnosis of extrapulmonary ***tuberculosis*** .
AU Munk, Martin E. (1); Arend, Sandra M.; Brock, Inger; Ottenhoff, Tom H. M.; ***Andersen, Peter***
CS (1) Dept. of Tuberculosis Immunology, States Serum Institute, 5, Artillerivej, 2300, Copenhagen S: mmn@ssi.dk Denmark
SO Journal of Infectious Diseases, (1 January, 2001) Vol. 183, No. 1, pp. 175-176. print.
ISSN: 0022-1899.
DT Letter
LA English
SL English

L6 ANSWER 2 OF 61 CAPLUS COPYRIGHT 2001 ACS
AN 2001:50676 CAPLUS
DN 134:114829
TI ***Tuberculosis*** vaccine and diagnostics based on the Mycobacterium ***tuberculosis*** esat-6 gene family
IN ***Andersen, Peter*** ; Skjot, Rikke
PA Statens Serum Institut, Den.
SO PCT Int. Appl., 80 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2001004151	A2	20010118	WO 2000-DK398	20000713

W: AE, AG, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH,

CN, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
PRAI DK 1999-1020 A 19990713
US 1999-144011 P 19990715
AB The authors report the cloning and T-cell-stimulatory activity of members of the esat-6 gene family of Mycobacterium ***tuberculosis*** .

L6 ANSWER 3 OF 61 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 1
AN 2001:302988 BIOSIS
DN PREV200100302988
TI Protection of mice with a ***tuberculosis*** subunit vaccine based on a fusion protein of antigen 85B and ESAT-6.
AU Olsen, Anja Weinreich; van Pinxteren, Laurens A. H.; Okkels, Limei Meng; Rasmussen, Peter Birk; ***Andersen, Peter (1)***
CS (1) Department of TB Immunology, Statens Serum Institut, Artillerivej 5, DK-2300, Copenhagen S: pa@ssi.dk Denmark
SO Infection and Immunity, (May, 2001) Vol. 69, No. 5, pp. 2773-2778. print. ISSN: 0019-9567.
DT Article
LA English
SL English
AB In this study, we investigated the potential of a ***tuberculosis*** subunit vaccine based on fusion proteins of the immunodominant antigens ESAT-6 and antigen 85B. When the fusion proteins were administered to mice in the adjuvant combination dimethyl dioctadecylammonium bromide-monophosphoryl lipid A, a strong dose-dependent immune response was induced to both single components as well as to the fusion proteins. The immune response induced was accompanied by high levels of protective immunity and reached the level of Mycobacterium bovis BCG-induced protection over a broad dose range. The vaccine induced efficient immunological memory, which remained stable 30 weeks postvaccination.

L6 ANSWER 4 OF 61 CAPLUS COPYRIGHT 2001 ACS
AN 2001:475998 CAPLUS
TI Preparation of culture filtrate proteins from Mycobacterium ***tuberculosis***
AU Rosenkrands, Ida; ***Andersen, Peter***
CS Department of TB Immunology, Statens Serum Institut, Copenhagen, Den.
SO Methods Mol. Med. (2001), 54(Mycobacterium tuberculosis Protocols), 205-215
CODEN: MMMEFN
PB Humana Press Inc.
DT Journal
LA English
AB Unavailable

L6 ANSWER 5 OF 61 CAPLUS COPYRIGHT 2001 ACS
AN 2001:271312 CAPLUS

DN 134:365388
TI TB vaccines: progress and problems
AU ***Andersen, Peter***
CS Dept of TB Immunology, Statens Seruminstitut, Copenhagen S, DK-2300, Den.
SO Trends Immunol. (2001), 22(3), 160-168
CODEN: TIRMAE; ISSN: 1471-4906
PB Elsevier Science Ltd.
DT Journal; General Review
LA English
AB A review with 77 refs. ***Tuberculosis*** (TB) is the biggest killer worldwide of any infectious disease, a situation worsened by the advent of the HIV epidemic and the emergence of multi-drug resistant strains of Mycobacterium ***tuberculosis*** . The existing vaccine, Mycobacterium bovis bacille Calmette-Guerin (BCG), has proven inefficient in several recent field trials. There is currently intense research using cutting-edge vaccine technol. to combat this ancient disease. However, it is necessary to understand why BCG has failed before the authors can rationally develop the next generation of vaccines. Several hypotheses that might explain the failure of BCG and the strategies designed to address these shortcomings are discussed.
RE.CNT 77
RE
(1) Andersen, P; Infect Immun 1991, V59, P1558 CAPLUS
(2) Andersen, P; Infect Immun 1994, V62, P2536 CAPLUS
(3) Andersen, P; Infect Immun 2000, V68, P621 CAPLUS
(4) Andersen, P; J Immunol 1995, V154, P3359 CAPLUS
(5) Andersen, P; Lancet 2000, V356, P1099 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 6 OF 61 BIOSIS COPYRIGHT 2001 BIOSIS
AN 2001:235031 BIOSIS
DN PREV200100235031
TI Use of ESAT-6 in the interferon-gamma test for diagnosis of bovine ***tuberculosis*** following skin testing.
AU Buddle, Bryce M. (1); Ryan, Terry J.; Pollock, John M.; ***Andersen,*** *** Peter*** ; de Lisle, Geoffrey W.
CS (1) Wallaceville Animal Research Centre, AgResearch, Upper Hutt: bryce.buddle@agresearch.co.nz New Zealand
SO Veterinary Microbiology, (3 May, 2001) Vol. 80, No. 1, pp. 37-46. print.
ISSN: 0378-1135.
DT Article
LA English
SL English
AB The whole blood interferon-gamma (IFN-gamma) test has proven to be a practical ancillary test for re-testing cattle for bovine ***tuberculosis*** 8-28 days following tuberculin skin testing. An improvement in the specificity of the IFN-gamma test could further reduce culling of false positive animals. The primary aim of this study was to evaluate a single mycobacterial antigen, ESAT-6 in the IFN-gamma test for use in skin test-positive cattle. These skin test-positive cattle comprised 51 Mycobacterium bovis-infected animals from ***tuberculosis*** -infected herds and 85 non-infected animals from ***tuberculosis*** -free herds. The test based on ESAT-6 had a higher specificity than the test based on purified protein derivative (PPD) tuberculin, but this was offset by a small decrease in sensitivity. Use of

a lower cut-off in the ESAT-6-based test improved the sensitivity, while still maintaining a very high specificity. A secondary aim in the study was to assess the ESAT-6 and PPD-based tests for detecting bovine ***tuberculosis*** in skin test-negative animals from a persistently infected herd. The PPD-based test detected the majority of the lesioned or M. bovis-culture positive animals, while the ESAT-6-based test detected a smaller proportion. The false negatives in the IFN-gamma test from both the skin test-negative and positive groups were predominantly M. bovis-culture positive animals with no visible lesions. The current study has shown that a defined specific antigen such as ESAT-6 can markedly improve the specificity of the IFN-gamma test for re-testing skin test-positive animals. An ESAT-6-based IFN-gamma test could be particularly useful to reduce the false positive rate, yet still maintain an acceptable level of sensitivity.

L6 ANSWER 7 OF 61 CAPLUS COPYRIGHT 2001 ACS
AN 2000:824123 CAPLUS
DN 134:4039
TI Adjuvant combinations for immunization composition and vaccines
IN Lindblad, Erik B.; Elhay, Martin J.; ***Andersen, Peter*** ; Brandt, Lise Ostergaard
PA Statens Serum Institut, Den.
SO PCT Int. Appl., 26 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2000069458	A2	20001123	WO 2000-DK251	20000512
WO 2000069458	A3	20010308		

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRAI DK 1999-655 A 19990512
AB The present invention relates to adjuvant combinations comprising two or more different adjuvants. In particular the invention relates to adjuvant compns. comprising a quaternary hydrocarbon ammonium halogenide and a hydrophobic second adjuvant component. The invention also relates to vaccines and immunization combination kits comprising two or more adjuvants and an antigenic substance, e.g. from Mycobacterium ***tuberculosis*** .

L6 ANSWER 8 OF 61 CAPLUS COPYRIGHT 2001 ACS
AN 2000:260319 CAPLUS
DN 132:292711
TI Tb vaccine and diagnostic based on antigens from the Mycobacterium ***tuberculosis*** cell
IN ***Andersen, Peter*** ; Weldingh, Karin; Hansen, Christina Veggerby;

Florio, Walter; Okkels, Li Mei Meng; Skjot, Rikke Louise Vinther; Rosenkrands, Ida
PA Statens Serum Institut, Den.
SO PCT Int. Appl., 126 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2000021983	A2	20000420	WO 1999-DK538	19991008
WO 2000021983	A3	20001123		

W: AE, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

AU 9960784	A1	20000501	AU 1999-60784	19991008
PRAI DK 1998-1281	A	19981008		
US 1999-116673	P	19990121		
WO 1999-DK538	W	19991008		

AB The present invention relates to substantially pure polypeptides, which has a sequence identity of at least 80 % to an amino acid sequence disclosed, or which is a subsequence of at least 6 amino acids thereof, preferably a B- or T-cell epitope of the polypeptides disclosed. The polypeptide or the subsequence thereof has at least one of nine properties. The use of the disclosed polypeptides in medicine is disclosed, preferably as vaccine or diagnostic agents relating to virulent Mycobacterium. The invention further relates to the nucleotide sequences disclosed and the nucleotide sequences encoding the disclosed polypeptides. Medical and non-medical use of the nucleotide sequences is disclosed.

L6 ANSWER 9 OF 61 CAPLUS COPYRIGHT 2001 ACS
AN 2001:374809 CAPLUS
TI Human CD8+ T cells specific for Mycobacterium ***tuberculosis*** secreted antigens in ***tuberculosis*** patients and healthy BCG-vaccinated controls in The Gambia
AU Smith, Steven M.; Klein, Michel R.; Malin, Adam S.; Sillah, Jackson; Huygen, Kris; ***Andersen, Peter*** ; McAdam, Keith P. W. J.; Dockrell, Hazel M.
CS Immunology Unit, London School of Hygiene and Tropical Medicine, London, WC1E 7HT, UK
SO Infect. Immun. (2000), 68(12), 7144-7148
CODEN: INFIBR; ISSN: 0019-9567
PB American Society for Microbiology
DT Journal
LA English
AB Intracellular flow cytometry anal. of perforin prodn. by CD8+ T cells showed levels were greatly reduced in ***tuberculosis*** (TB) patients compared to healthy controls. Reduced cytotoxic-T-lymphocyte activity was

also obtained with CD8+ T cells from TB patients compared to healthy controls in The Gambia. A change in antigen recognition was noted between the two groups of donors: in addn. to recognition of Ag85A and Ag85B, as seen in healthy donors, a prominent ESAT-6 response was found in TB patients.

RE.CNT 26

RE

(1) Andersen, P; J Immunol 1995, V154, P3359 CAPLUS

(3) Cooper, A; Infect Immun 1997, V65, P1317 CAPLUS

(4) Denis, O; Infect Immun 1997, V65, P676 CAPLUS

(5) Denis, O; Infect Immun 1998, V66, P1527 CAPLUS

(6) Denis, O; Int Immunol 1999, V11, P209 CAPLUS

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 10 OF 61 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 2

AN 2001:37127 BIOSIS

DN PREV200100037127

TI Towards the proteome of Mycobacterium ***tuberculosis*** .

AU Rosenkrands, Ida (1); King, Angus; Weldingh, Karin; Moniatte, Marc; Moertz, Ejvind; ***Andersen, Peter***

CS (1) Department of TB Immunology, Statens Serum Institut, 5 Artillerivej, DK-2300, Copenhagen S: idr@ssi.dk Denmark

SO Electrophoresis, (November, 2000) Vol. 21, No. 17, pp. 3740-3756. print. ISSN: 0173-0835.

DT Article

LA English

SL English

AB Human ***tuberculosis*** is caused by the intracellular pathogen Mycobacterium ***tuberculosis*** . Sequencing of the genome of M. ***tuberculosis*** strain H37Rv has predicted 3924 open reading frames, and enabled identification of proteins from this bacterium by peptide mass fingerprinting. Extracellular proteins from the culture medium and proteins in cellular extracts were examined by two-dimensional gel electrophoresis using immobilized pH gradient technology. By mass spectrometry and immunodetection, 49 culture filtrate proteins and 118 lysate proteins were identified, 83 of which were novel. To date, 288 proteins have been identified in M. ***tuberculosis*** proteome studies, and a list is presented which includes all identified proteins (available at http://www.ssi.dk/publichealth/tbimmun). The information obtained from the M. ***tuberculosis*** proteome so far is discussed in relation to the information obtained from the complete genome sequence.

L6 ANSWER 11 OF 61 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 3

AN 2001:62081 BIOSIS

DN PREV200100062081

TI Control of latent Mycobacterium ***tuberculosis*** infection is dependent on CD8 T cells.

AU van Pinxteren, Laurens A. H.; Cassidy, Joseph P.; Smedegaard, Birgitte H. C.; Agger, Else M.; ***Andersen, Peter (1)***

CS (1) Department of TB Immunology, Statens Serum Institute, Artillerivej, DK-2300, Copenhagen S: pa@ssi.dk Denmark

SO European Journal of Immunology, (December, 2000) Vol. 30, No. 12, pp. 3689-3698. print.
ISSN: 0014-2980.

DT Article

LA English
SL English
AB It is estimated that one-third of the world's population is infected with Mycobacterium ***tuberculosis*** , but that only 10% of infected people break down with the disease. In the remaining 90% the infection remains clinically latent. In the present study, the immune mechanisms controlling the latent phase of ***tuberculosis*** infection were evaluated in a mouse model of latency and reactivation. Mice aerosol-infected with M. ***tuberculosis*** were treated with anti-mycobacterial drugs resulting in very low, stable bacterial numbers (<500 CFU in the spleen and lung) for 10-12 weeks followed by reactivation of the disease with increasing bacterial numbers. During latency, pathological changes in the lung had almost completely resolved and lymphocyte number and turnover were at the pre-infection level. The CD4 subset was highly active during the acute phase of infection and could be detected by intracellular staining for IFN-gamma as well as after antigen-specific stimulation with mycobacterial antigens. The CD8 subset was not involved in the acute stage of infection, but this subset was active and produced IFN-gamma during the latent phase of infection. In vivo depletion of T cell subsets supported these findings with a 6-7-fold increase in bacterial numbers in the lung following anti-CD4 treatment during the acute phase, while anti-CD8 treatment did not have an effect. The opposite was found during the latent phase where anti-CD8 treatment as well as anti-IFN-gamma treatment both resulted in a 10-fold increase in bacterial numbers in the lung, while anti-CD4 treatment induced only a modest change.

L6 ANSWER 12 OF 61 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 4
AN 2000:282183 BIOSIS
DN PREV200000282183
TI Antigenic equivalence of human T-cell responses to Mycobacterium ***tuberculosis*** -specific RD1-encoded protein antigens ESAT-6 and culture filtrate protein 10 and to mixtures of synthetic peptides.
AU Arend, Sandra M.; Geluk, Annemieke; van Meijgaarden, Krista E.; van Dissel, Jaap T.; Theisen, Michael; ***Andersen, Peter*** ; Ottenhoff, Tom H. M.
SO Infection and Immunity, (June, 2000) Vol. 68, No. 6, pp. 3314-3321. print..
ISSN: 0019-9567.
DT Article
LA English
SL English
AB The early secreted antigenic target 6-kDa protein (ESAT-6) and culture filtrate protein 10 (CFP-10) are promising antigens for reliable immunodiagnosis of ***tuberculosis*** . Both antigens are encoded by RD1, a genomic region present in all strains of Mycobacterium ***tuberculosis*** and M. bovis but lacking in all M. bovis bacillus Calmette-Guerin vaccine strains. Production and purification of recombinant antigens are laborious and costly, precluding rapid and large-scale testing. Aiming to develop alternative diagnostic reagents, we have investigated whether recombinant ESAT-6 (rESAT-6) and recombinant CFP-10 can be replaced with corresponding mixtures of overlapping peptides spanning the complete amino acid sequence of each antigen. Proliferation of M. ***tuberculosis*** -specific human T-cell lines in response to rESAT-6 and rCFP-10 and that in response to the corresponding peptide mixtures were almost completely correlated ($r = 0.96$, $P < 0.0001$ for

ESAT-6; r = 0.98, P < 0.0001 for CFP-10). More importantly, the same was found when gamma interferon production by peripheral blood mononuclear cells in response to these stimuli was analyzed (r = 0.89, P < 0.0001 for ESAT-6; r = 0.89, P < 0.0001 for CFP-10). Whole protein antigens and the peptide mixtures resulted in identical sensitivity and specificity for detection of infection with M. ***tuberculosis*** . The peptides in each mixture contributing to the overall response varied between individuals with different HLA-DR types. Interestingly, responses to CFP-10 were significantly higher in the presence of HLA-DR15, which is the major subtype of DR2. These results show that mixtures of synthetic overlapping peptides have potency equivalent to that of whole ESAT-6 and CFP-10 for sensitive and specific detection of infection with M. ***tuberculosis*** , and peptides have the advantage of faster production at lower cost.

L6 ANSWER 13 OF 61 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 5
AN 2000:349404 BIOSIS
DN PREV200000349404
TI Detection of active ***tuberculosis*** infection by T cell responses to early-secreted antigenic target 6-kDa protein and culture filtrate protein 10.
AU Arend, Sandra M. (1); ***Andersen, Peter*** ; van Meijgaarden, Krista E.; Skjot, Rikke L. V.; Subronto, Yanri W.; van Dissel, Jaap T.; Ottenhoff, Tom H. M.
CS (1) Dept. of Infectious Diseases, C5P, Leiden University Medical Center, 2300 RC, Leiden Netherlands
SO Journal of Infectious Diseases, (May, 2000) Vol. 181, No. 5, pp. 1850-1854. print.
ISSN: 0022-1899.
DT Article
LA English .
SL English
AB The purified protein derivative (PPD) skin test has no predictive value for ***tuberculosis*** (TB) in Mycobacterium bovis bacillus Calmette-Guerin (BCG)-vaccinated individuals because of cross-reactive responses to nonspecific constituents of PPD. T cell responses to early-secreted antigenic target 6-kDa protein (ESAT-6) and the newly identified culture filtrate protein 10 (CFP-10), 2 proteins specifically expressed by M. ***tuberculosis*** (MTB) but not by BCG strains, were evaluated. Most TB patients responded to ESAT-6 (92%) or CFP-10 (89%). A minority of BCG-vaccinated individuals responded to both ESAT-6 and CFP-10, their history being consistent with latent infection with MTB in the presence of protective immunity. No responses were found in PPD-negative controls. The sensitivity and specificity of the assay were 84% and 100%, respectively, at a cutoff of 300 pg of interferon-gamma/mL. These data indicate that ESAT-6 and CFP-10 are promising antigens for highly specific immunodiagnosis of TB, even in BCG-vaccinated individuals.

L6 ANSWER 14 OF 61 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 6
AN 2000:314973 BIOSIS
DN PREV200000314973
TI Efficient protection against Mycobacterium ***tuberculosis*** by vaccination with a single subdominant epitope from the ESAT-6 antigen.
AU Olsen, Anja Weinreich; Hansen, Paul Robert; Holm, Arne; ***Andersen,*** *** Peter***

SO European Journal of Immunology, (June, 2000) Vol. 30, No. 6, pp. 1724-1732. print.
ISSN: 0014-2980.
DT Article
LA English
SL English
AB We have investigated the vaccine potential of two peptides derived from the 6-kDa early secretory antigenic target (ESAT)-6 antigen in the mouse model of ***tuberculosis*** . The peptides were both strongly immunogenic in B6CBAF1 (H-2b,k) mice and primed recall responses of the same intensity after immunization. However, both ***tuberculosis*** infection and immunization with ESAT-6 resulted in responses focused towards ESAT-61-20. Multiple antigen peptide constructs as well as free peptides were emulsified with dimethyl dioctade-cylammonium bromide/monophosphoryl lipid A/IL-2 and tested as experimental vaccines in an i.v. and aerosol model of ***tuberculosis*** in mice. The peptide were highly immunogenic and induced cellular responses of the same magnitude. However, only vaccines based on the subdominant ESAT-651-70 epitope promoted significant levels of protective immunity and the level of protection was equivalent to that achieved with ESAT-6 and BCG. These findings demonstrate the potential of peptide-based vaccines against ***tuberculosis*** and indicate that there is not direct correlation between the hierarchy of response to naturally processed peptides and their ability to induce protective immunity against Mycobacterium ***tuberculosis*** .

L6 ANSWER 15 OF 61 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 7
AN 2001:116487 BIOSIS
DN PREV200100116487
TI Vaccinia expression of Mycobacterium ***tuberculosis*** -secreted proteins: Tissue plasminogen activator signal sequence enhances expression and immunogenicity of M. ***tuberculosis*** Ag85.
AU Malin, Adam S. (1); Huygen, Kris; Content, Jean; Mackett, Michael; Brandt, Lisa; ***Andersen, Peter*** ; Smith, Steven M.; Dockrell, Hazel M.
CS (1) Royal United Hospital, Bath, BA1 3NG: adam.malin@bigfoot.com UK
SO Microbes and Infection, (November, 2000) Vol. 2, No. 14, pp. 1677-1685. print.
ISSN: 1286-4579.
DT Article
LA English
SL English
AB There is increasing evidence to implicate a role for CD8+ T cells in protective immunity against ***tuberculosis*** . Recombinant vaccinia (rVV) expressing Mycobacterium ***tuberculosis*** (MTB) proteins can be used both as tools to dissect CD8+ T-cell responses and, in attenuated form, as candidate vaccines capable of inducing a balanced CD4+/CD8+ T-cell response. A panel of rVV was constructed to express four immunodominant secreted proteins of MTB: 85A, 85B and 85C and ESAT-6. A parallel group of rVV was constructed to include the heterologous eukaryotic tissue plasminogen activator (tPA) signal sequence to assess if this would enhance expression and immunogenicity. Clear expression was obtained for 85A, 85B and ESAT-6 and the addition of tPA resulted in N-glycosylation and a 4-10-fold increase in expression. Female C57BL/6 mice were immunised using the rVV-Ag85 constructs, and interleukin-2 and gamma-interferon were assayed using a co-culture of immune splenocytes and

recall antigen. There was a marked increase in cytokine production in mice immunised with the tPA-containing constructs. We report the first data demonstrating enhanced immunogenicity of rVV using a tPA signal sequence, which has significant implications for future vaccine design.

L6 ANSWER 16 OF 61 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 8
AN 2000:271567 BIOSIS
DN PREV200000271567
TI Mapping and identification of Mycobacterium ***tuberculosis*** proteins by two-dimensional gel electrophoresis, microsequencing and immunodetection.
AU Rosenkrands, Ida; Weldingh, Karin; Jacobsen, Susanne; Hansen, Christina Veggerby; Florio, Walter; Gianetri, Isabella; ***Andersen, Peter (1)***
CS (1) Department of TB Immunology, Statens Serum Institute, 5 Artillerivej, DK-2300, Copenhagen S Denmark
SO Electrophoresis, (March, 2000) Vol. 21, No. 5, pp. 935-948. print.. ISSN: 0173-0835.
DT Article
LA English
SL English
AB Mycobacterium ***tuberculosis*** is the infectious agent giving rise to human ***tuberculosis*** . The entire genome of M. ***tuberculosis*** , comprising approximately 4000 open reading frames, has been sequenced. The huge amount of information released from this project has facilitated proteome analysis of M. ***tuberculosis*** . Two-dimensional polyacrylamide gel electrophoresis (2-D PAGE) was applied to fractions derived from M. ***tuberculosis*** culture filtrate, cell wall, and cytosol, resulting in the resolution of 376, 413, and 395 spots, respectively, in silver-stained gels. By microsequencing and immunodetection, 38 culture filtrate proteins were identified and mapped, of which 12 were identified for the first time. In the same manner, 23 cell wall proteins and 19 cytosol proteins were identified and mapped, with 9 and 10, respectively, being novel proteins. One of the novel proteins was not predicted in the genome project, and for four of the identified proteins alternative start codons were suggested. Fourteen of the culture filtrate proteins were proposed to possess signal sequences. Seven of these proteins were microsequenced and the N-terminal sequences obtained confirmed the prediction. The data presented here are an important complement to the genetic information, and the established 2-D PAGE maps (also available at: www.ssi.dk/publichealth/tbimmun) provide a basis for comparative studies of protein expression.

L6 ANSWER 17 OF 61 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 9
AN 2000:110101 BIOSIS
DN PREV200000110101
TI ESAT-6 subunit vaccination against Mycobacterium ***tuberculosis*** .
AU Brandt, Lise; Elhay, Martin; Rosenkrands, Ida; Lindblad, Erik B.; ***Andersen, Peter (1)***
CS (1) Department of TB Immunology, Statens Serum Institut, Artillerivej 5, 2300, Copenhagen S. Denmark
SO Infection and Immunity, (Feb., 2000) Vol. 68, No. 2, pp. 791-795. ISSN: 0019-9567.
DT Article
LA English
SL English

AB The ESAT-6 antigen from Mycobacterium ***tuberculosis*** is a dominant target for cell-mediated immunity in the early phase of ***tuberculosis*** (TB) in TB patients as well as in various animal models. The purpose of our study was to evaluate the potential of ESAT-6 in an experimental TB vaccine. We started out using dimethyl dioctadecylammonium bromide (DDA), an adjuvant which has been demonstrated to be efficient for the induction of cellular immune responses and has been used successfully before as a delivery system for TB vaccines. Here we demonstrate that, whereas immune responses to both short-term-culture filtrate and AG85B are efficiently induced with DDA, this adjuvant was inefficient for the induction of immune responses to ESAT-6. Therefore, we investigated the modulatory effect of monophosphoryl lipid A (MPL), an immunomodulator which in different combinations has demonstrated strong adjuvant activity for both cellular and humoral immune responses. We show in the present study that vaccination with ESAT-6 delivered in a combination of MPL and DDA elicited a strong ESAT-6-specific T-cell response and protective immunity comparable to that achieved with Mycobacterium bovis BCG.

L6 ANSWER 18 OF 61 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 10
AN 2000:104851 BIOSIS
DN PREV200000104851
TI CD4+ T-cell subsets that mediate immunological memory to Mycobacterium ***tuberculosis*** infection in mice.
AU ***Andersen, Peter (1)*** ; Smedegaard, Birgitte
CS (1) Department of TB Immunology, Statens Serum Institut, 5 Artillerivej, Copenhagen Denmark
SO Infection and Immunity, (Feb., 2000) Vol. 68, No. 2, pp. 621-629. ISSN: 0019-9567.
DT Article
LA English
SL English
AB We have studied CD4+ T cells that mediate immunological memory to an intravenous infection with Mycobacterium ***tuberculosis*** . The studies were conducted with a mouse model of memory immunity in which mice are rendered immune by a primary infection followed by antibiotic treatment and rest. Shortly after reinfection, ***tuberculosis*** -specific memory cells were recruited from the recirculating pool, leading to rapidly increasing precursor frequencies in the liver and a simultaneous decrease in the blood. A small subset of the infiltrating T cells was rapidly activated (<20 h) and expressed high levels of intracellular gamma interferon and the T-cell activation markers CD69 and CD25. These memory effector T cells expressed intermediate levels of CD45RB and were heterogeneous with regard to the L-selectin and CD44 markers. By adoptive transfer into nude mice, the highest level of resistance to a challenge with M. ***tuberculosis*** was mediated by CD45RBhigh, L-selectinhigh, CD44low cells. Taken together, these two lines of evidence support an important role for memory cells which have reverted to a naive phenotype in the long-term protection against M. ***tuberculosis*** .

L6 ANSWER 19 OF 61 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 11
AN 2000:104643 BIOSIS
DN PREV200000104643
TI Comparative evaluation of low-molecular-mass proteins from Mycobacterium

tuberculosis identifies members of the ESAT-6 family as immunodominant T-cell antigens.

AU Skjot, Rikke Louise Vinther; Oettinger, Thomas; Rosenkrands, Ida; Ravn, Pernille; Brock, Inger; Jacobsen, Susanne; ***Andersen, Peter (1)***

CS (1) Department of TB Immunology, Statens Serum Institut, Artillerivej 5, DK-2300, Copenhagen S Denmark

SO Infection and Immunity, (Jan., 2000) Vol. 68, No. 1, pp. 214-220. ISSN: 0019-9567.

DT Article

LA English

SL English

AB Culture filtrate from Mycobacterium ***tuberculosis*** contains protective antigens of relevance for the generation of a new antituberculosis vaccine. We have identified two previously uncharacterized M. ***tuberculosis*** proteins (TB7.3 and TB10.4) from the highly active low-mass fraction of culture filtrate. The molecules were characterized, mapped in a two-dimensional electrophoresis reference map of short-term culture filtrate, and compared with another recently identified low-mass protein, CFP10 (F. X. Berthet, P. B. Rasmussen, I. Rosenkrands, P. Andersen, and B. Gicquel. Microbiology 144:3195-3203, 1998), and the well-described ESAT-6 antigen. Genetic analyses demonstrated that TB10.4 as well as CFP10 belongs to the ESAT-6 family of low-mass proteins, whereas TB7.3 is a low-molecular-mass protein outside this family. The proteins were expressed in Escherichia coli, and their immunogenicity was tested in cultures of peripheral blood mononuclear cells from human ***tuberculosis*** (TB) patients, Mycobacterium bovis BCG-vaccinated donors, and nonvaccinated donors. The two ESAT-6 family members, TB10.4 and CFP10, were very strongly recognized and induced gamma interferon release at the same level (CFP10) as or at an even higher level (TB10.4) than ESAT-6. The non-ESAT-6 family member, TB7.3, for comparison, was recognized at a much lower level. CFP10 was found to distinguish TB patients from BCG-vaccinated donors and is, together with ESAT-6, an interesting candidate for the diagnosis of TB. The striking immunodominance of antigens within the ESAT-6 family is discussed, and hypotheses are presented to explain this targeting of the immune response during TB infection.

L6 ANSWER 20 OF 61 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 12

AN 2000:157810 BIOSIS

DN PREV200000157810

TI Diagnosis of ***tuberculosis*** based on the two specific antigens ESAT-6 and CFP10.

AU van Pinxteren, Laurens A. H.; Ravn, Pernille; Agger, Else Marie; Pollock, John; ***Andersen, Peter (1)***

CS (1) Department of TB-Immunology, Statens Serum Institut, Artillerivej 5, 2300, Copenhagen S Denmark

SO Clinical and Diagnostic Laboratory Immunology., (March, 2000) Vol. 7, No. 2, pp. 155-160.
ISSN: 1071-412X.

DT Article

LA English

SL English

AB Tests based on tuberculin purified protein derivative (PPD) cannot distinguish between ***tuberculosis*** infection, Mycobacterium bovis BCG vaccination, or exposure to environmental mycobacteria. The present

study investigated the diagnostic potential of two Mycobacterium ***tuberculosis*** -specific antigens (ESAT-6 and CFP10) in experimental animals as well as during natural infection in humans and cattle. Both antigens were frequently recognized in vivo and in vitro based on the induction of delayed-type hypersensitivity responses and the ability to induce gamma interferon production by lymphocytes, respectively. The combination of ESAT-6 and CFP10 was found to be highly sensitive and specific for both in vivo and in vitro diagnosis. In humans, the combination had a high sensitivity (73%) and a much higher specificity (93%) than PPD (7%).

L6 ANSWER 21 OF 61 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 13
AN 2000:10612 BIOSIS
DN PREV200000010612
TI ***Tuberculosis*** vaccine.
AU ***Andersen, Peter (1)*** ; Andersen, NG.se Bengaard; Haslov, Kaare; Sorensen, Anne Lund
CS (1) Bronshoj Denmark
ASSIGNEE: Statens Seruminstitut
PI US 5955077 Sep. 21, 1999
SO Official Gazette of the United States Patent and Trademark Office Patents, (Sep. 21, 1999) Vol. 1226, No. 3, pp. No pagination.
ISSN: 0098-1133.
DT Patent
LA English

L6 ANSWER 22 OF 61 CAPLUS COPYRIGHT 2001 ACS
AN 1999:77692 CAPLUS
DN 130:165432
TI The antigenic protein LHP of Mycobacterium ***tuberculosis*** and the lhp gene encoding it and their diagnostic and prophylactic uses
IN Gicquel, Brigitte; Berthet, Francois-Xavier; ***Andersen, Peter*** ; Rasmussen, Peter Birk
PA Institut Pasteur, Fr.; Statens Serum Institut
SO PCT Int. Appl., 88 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9904005	A1	19990128	WO 1998-IB1091	19980716
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9881238	A1	19990210	AU 1998-81238	19980716
EP 1003870	A1	20000531	EP 1998-930967	19980716
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
PRAI US 1997-52631	P	19970716		

WO 1998-IB1091 W 19980716

AB The Mycobacterium ***tuberculosis*** gene encoding the antigenic protein LHP that is homologous to the L45 antigen of M. bovis, is cloned and characterized. The gene can be expressed from its own promoter in slow-growing (M. ***tuberculosis*** group) and fast-growing (M. smegmatis) mycobacteria. The LHP gene product, and antigenic peptides derived from it, can be manufd. for use in vaccines and to raise reagent antibodies for diagnostic use. The promoter of the lhp gene may be of use in the expression of foreign genes in Mycobacteria. Oligonucleotides derived from the promoter region may be useful as probes or primers in the detection of M. ***tuberculosis*** in a biol. sample. Anal. of the promoters driving expression of the closely linked lhp and orf1C genes of M. ***tuberculosis*** established that they form an operon. Use of the promoter to drive expression of a reporter gene in M. smegmatis is demonstrated. The protein is abundant in short-term (7 day) culture filtrates of M. ***tuberculosis*** .

RE.CNT 9

RE

(1) Ajinomoto Kk; EP 0400973 A 1990 CAPLUS

(3) Corixa Corp; WO 9709428 A 1997 CAPLUS

(4) Corixa Corp; WO 9709429 A 1997 CAPLUS

(5) Corixa Corp; WO 9816645 A 1998 CAPLUS

(6) Corixa Corp; WO 9816646 A 1998 CAPLUS

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L6 ANSWER 23 OF 61 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 14

AN 2000:34137 BIOSIS

DN PREV200000034137

TI T-cell recognition of Mycobacterium ***tuberculosis*** culture filtrate fractions in ***tuberculosis*** patients and their household contacts.

AU Demissie, Abebech; Ravn, Pernille; Olobo, Joseph; Doherty, T. Mark; Eguale, Tewodros; Geletu, Mulu; Hailu, Wondewossen; ***Andersen, Peter*** *** (1)*** ; Britton, Sven

CS (1) Statens Seruminstitut, 5 Artillerivej, Copenhagen, 2300 S Denmark

SO Infection and Immunity, (Nov., 1999) Vol. 67, No. 11, pp. 5967-5971. ISSN: 0019-9567.

DT Article

LA English

SL English

AB We examined the immune responses of patients with active pulmonary ***tuberculosis*** (TB) and their healthy household contacts to short-term culture filtrate (ST-CF) of Mycobacterium ***tuberculosis*** or molecular mass fractions derived from it. Our goal was to identify fractions strongly recognized by donors and differences among the donor groups of possible relevance for vaccine development. The study population consisted of 65 human immunodeficiency virus-negative donors from the Hossana Regional Hospital, Hossana, Ethiopia. Peripheral blood leukocytes from the donors were stimulated with different antigens and immune responses were determined. Household contacts produced significantly higher levels of gamma interferon (IFN-gamma) than the TB patients in response to antigens present in ST-CF and the 10 narrow-molecular-mass fractions. A similar difference in leukocyte proliferative responses to the antigens between the two groups was also found. In general, while all fractions stimulated immune responses, the highest activity was seen with

the low-molecular-mass fractions, which include well-defined TB antigens such as ESAT-6. Leukocytes from contacts of TB patients with severe disease produced higher levels of antigen-specific IFN-gamma than those from contacts of patients with minimal disease. Both groups of contacts exhibited higher cell-mediated responses than the patients themselves. The enhanced immune response of healthy contacts, especially those of patients with severe disease, to secreted mycobacterial antigens is suggestive of an early stage of infection by M. ***tuberculosis*** , which could in time result in overt disease or containment of the infection. This possibility is currently being investigated by follow-up studies of the household contacts.

L6 ANSWER 24 OF 61 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 15
AN 2000:36059 BIOSIS
DN PREV200000036059
TI Interleukin-6 and interleukin-12 participate in induction of a type 1 protective T-cell response during vaccination with a ***tuberculosis*** subunit vaccine.
AU Leal, Irene S.; Smedegard, Birgitte; ***Andersen, Peter*** ; Appelberg, Rui (1)
CS (1) Laboratory of Microbiology and Immunology of Infection, Institute for Molecular and Cell Biology, Rua do Campo Alegre 823, 4150, Porto Portugal
SO Infection and Immunity, (Nov., 1999) Vol. 67, No. 11, pp. 5747-5754. ISSN: 0019-9567.
DT Article
LA English
SL English
AB We examined the role of cytokines in the development of gamma interferon (IFN-gamma)-secreting protective T cells following immunization with a culture filtrate subunit vaccine against Mycobacterium ***tuberculosis*** containing the adjuvant dimethyldioctadecylammonium bromide (DDA). Depletion of either interleukin-6 (IL-6) or IL-12 with specific neutralizing antibodies during vaccination reduced the priming of T cells for antigen-specific proliferation and IFN-gamma secretion. Such reduction was also observed in IL-6 gene-disrupted mice as compared to wild-type animals. IL-6 was found to play a role in the initial differentiation of Th1 cells but not in their expansion. The defect found after IL-6 depletion or in IL-6-knockout mice was compensated by the inclusion of recombinant mouse IL-12 in the vaccine. The induction of protective immunity against an intravenous or an aerosol challenge with live, virulent M. ***tuberculosis*** was markedly reduced by neutralizing either IL-6 or IL-12 during immunization with the vaccine. Likewise, the effects of IL-6 neutralization were partially reversed by including IL-12 in the vaccine. Our data point to an important role of IL-6 and IL-12 in the generation of cell-mediated immunity to ***tuberculosis*** .

L6 ANSWER 25 OF 61 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 16
AN 2000:34114 BIOSIS
DN PREV200000034114
TI Differential T-cell recognition of native and recombinant Mycobacterium ***tuberculosis*** GroES.
AU Rosenkrands, Ida; Weldingh, Karin; Ravn, Pernille; Brandt, Lise; Hojrup, Peter; Rasmussen, Peter Birk; Coates, Anthony R.; Singh, Mahavir; Mascagni, Paolo; ***Andersen, Peter (1)***

CS (1) Department of TB Immunology, Statens Serum Institut, 5 Artillerivej, DK-2300, Copenhagen S Denmark

SO Infection and Immunity, (Nov., 1999) Vol. 67, No. 11, pp. 5552-5558. ISSN: 0019-9567.

DT Article

LA English

SL English

AB Mycobacterium ***tuberculosis*** GroES was purified from culture filtrate, and its identity was confirmed by immunoblot analysis and N-terminal sequencing. Comparing the immunological recognition of native and recombinant GroES, we found that whereas native GroES elicited a strong proliferative response and release of gamma interferon-gamma by peripheral blood mononuclear cells from healthy tuberculin reactors, the recombinant protein failed to do so. The same difference in immunological recognition was observed in a mouse model of TB infection. Both the native and recombinant preparations were recognized by mice immunized with the recombinant protein. Biochemical characterization including sodium dodecyl sulfate-polyacrylamide gel electrophoresis, two-dimensional electrophoresis, and mass spectrometry analysis of both proteins demonstrated no differences between the native and recombinant forms of GroES except for the eight additional N-terminal amino acids derived from the fusion partner inrecombinant GroES. The recombinant fusion protein, still tagged with the maltose binding protein, was recognized by T cells isolated from TB-infected mice if mixed with culture filtrate before affinity purification on an amylose column. The maltose binding protein treated in the same manner as a control preparation was not recognized. Based on the data presented, we suggest that the association of biologically active molecules from culture filtrate with the chaperone GroES may be responsible for the observed T-cell recognition of the native preparation.

L6 ANSWER 26 OF 61 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 17

AN 1999:197118 BIOSIS

DN PREV199900197118

TI Human T cell responses to the ESAT-6 antigen from Mycobacterium ***tuberculosis*** .

AU Ravn, Pernille; Demissie, Abebech; Eguale, Tewodros; Wondwosson, Hailu; Lein, David; Amoudy, Hanady A.; Mustafa, Abu S.; Jensen, Axel Kok; Holm, Arne; Rosenkrands, Ida; Oftung, Fredrik; Olobo, Joseph; von Reyn, Fordham; ***Andersen, Peter (1)***

CS (1) Dept. of TB Immunology, Statens Serum Institut, Artillerivej 5, 2300 S Denmark

SO Journal of Infectious Diseases, (March, 1999) Vol. 179, No. 3, pp. 637-645.
ISSN: 0022-1899.

DT Article

LA English

AB Human T cell responses to ESAT-6 and eight synthetic overlapping peptides were investigated in ***tuberculosis*** (TB) patients and control subjects from regions of high and low endemicity for TB. ESAT-6 was recognized by 65% of all tuberculin purified protein derivative-responsive TB patients, whereas only 2 of 29 bacille Calmette-Guerin-vaccinated Danish healthy donors recognized this molecule. In Ethiopia, a high frequency (58%) of healthy contacts of TB patients recognized ESAT-6. All of the peptides were recognized by some donors, indicating that the

molecule holds multiple epitopes. Danish and Ethiopian patients differed in the fine specificity of their peptide responses. Recognition of the C-terminal region (aa 72-95) was predominant in Danish patients, whereas recognition of aa 42-75 was predominant in Ethiopia. The relationship of these differences to the distribution of HLA types in the two populations is discussed. This study demonstrates that ESAT-6 is frequently recognized during early infection and holds potential as a component of a future TB-specific diagnostic reagent.

L6 ANSWER 27 OF 61 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 18
AN 1999:360427 BIOSIS
DN PREV199900360427
TI Cellular immune responses to ESAT-6 discriminate between patients with pulmonary disease due to Mycobacterium avium complex and those with pulmonary disease due to Mycobacterium ***tuberculosis*** .
AU Lein, A. David (1); von Reyn, C. Fordham; Ravn, Pernille; Horsburgh, C. Robert, Jr.; Alexander, Lorraine N.; ***Andersen, Peter***
CS (1) Section of Infectious Diseases, Dartmouth-Hitchcock Medical Center, Lebanon, NH, 03756 USA
SO Clinical and Diagnostic Laboratory Immunology, (July, 1999) Vol. 6, No. 4, pp. 606-609.
ISSN: 1071-412X.
DT Article
LA English
SL English
AB ESAT-6 (for 6-kDa early secreted antigenic target) is a secreted antigen found almost exclusively in organisms of the Mycobacterium ***tuberculosis*** complex. We compared in vitro gamma interferon (IFN-gamma) responses by peripheral blood mononuclear cells to this antigen in patients with pulmonary disease due to either Mycobacterium avium complex (MAC) or Mycobacterium ***tuberculosis*** with those in healthy, skin test-negative, control subjects. Significant IFN-gamma responses to ESAT-6 were detected in 16 (59%) of 27 M. ***tuberculosis*** pulmonary disease patients, 0 (0%) of 8 MAC disease patients, and 0 (0%) of 8 controls. Significant IFN-gamma responses to M. ***tuberculosis*** purified protein derivative were detected in 23 (85%) of 27 M. ***tuberculosis*** disease patients, 2 (25%) of 8 MAC disease patients, and 5 (63%) of 8 healthy controls. M. avium sensitin was recognized in 24 (89%) of 27 M. ***tuberculosis*** disease patients, 4 (50%) of 8 MAC disease patients, and 1 (13%) of 8 controls. IFN-gamma responses to ESAT-6 are specific for disease due to M. ***tuberculosis*** and are not observed in patients with MAC disease or in healthy controls.

L6 ANSWER 28 OF 61 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 19
AN 1999:146249 BIOSIS
DN PREV199900146249
TI Immunological evaluation of novel Mycobacterium ***tuberculosis*** culture filtrate proteins.
AU Weldingh, Karin; ***Andersen, Peter (1)***
CS (1) Dep. TB Immunol., Statens Serum Inst., Artillerivej 5, DK-2300 Copenhagen S Denmark
SO FEMS Immunology and Medical Microbiology, (Feb., 1999) Vol. 23, No. 2, pp. 159-164.
ISSN: 0928-8244.

DT Article
LA English
AB Culture filtrate from Mycobacterium ***tuberculosis*** contains molecules which can promote protective immunity to ***tuberculosis*** in animal models. Six novel proteins in the region of 17-29 kDa were purified and investigated for their immunological relevance in M. ***tuberculosis*** -infected mice, guinea pigs and ***tuberculosis*** patients. The proteins CFP17, CFP21, CFP25 and CFP29 were all identified as strong interferon-gamma inducers in M. ***tuberculosis*** -infected mice and in ***tuberculosis*** patients. The CFP21 protein is encoded in the genomic region RD-2 which is deleted from a number of BCG strains and the diagnostic potential of this antigen was evaluated.

L6 ANSWER 29 OF 61 BIOSIS COPYRIGHT 2001 BIOSIS
AN 2000:139578 BIOSIS
DN PREV200000139578
TI TB diagnosis based on two specific antigens ESAT-6 and CFP10.
AU van Pinxteren, Laurens A. H. (1); Ravn, Pernille (1); Pollock, John; ***Andersen, Peter (1)***
CS (1) Department of TB-Immunology, Statens Serum Institute, Artillerivej 5, 2300, Copenhagen S Denmark
SO Immunology., (Dec., 1999) Vol. 98, No. suppl. 1, pp. 40.
Meeting Info.: Joint Congress of the British Society for Immunology and the British Society for Allergy & Clinical Immunology. Harrogate, England, UK November 30-December 03, 1999 British Society for Allergy & Clinical Immunology
. ISSN: 0019-2805.
DT Conference
LA English
SL English

L6 ANSWER 30 OF 61 BIOSIS COPYRIGHT 2001 BIOSIS
AN 1999:99338 BIOSIS
DN PREV199900099338
TI Differentiation between Mycobacterium bovis BCG-vaccinated and M. bovis-infected cattle by using recombinant mycobacterial antigens.
AU Buddle, Bryce C. (1); Parlane, Natalie A.; Keen, Denise L.; Aldwell, Frank E.; Pollock, John M.; Lightbody, Ken; ***Andersen, Peter***
CS (1) AgRes., Wallaceville Anim. Res. Cent., P.O. Box 40-063, Upper Hutt New Zealand
SO Clinical and Diagnostic Laboratory Immunology, (Jan., 1999) Vol. 6, No. 1, pp. 1-5.
ISSN: 1071-412X.
DT Article
LA English
AB ***Tuberculosis*** continues to be a worldwide problem for both humans and animals. The development of tests to differentiate between infection with Mycobacterium ***tuberculosis*** or Mycobacterium bovis and vaccination with M. bovis BCG could greatly assist in the diagnosis of early infection as well as enhance the use of ***tuberculosis*** vaccines on a wider scale. Recombinant forms of four major secreted proteins of M. bovis-MPB59, MPB64, MPB70, and ESAT-6-were tested in a whole-blood gamma interferon (IFN-gamma) assay for differentiation between cattle vaccinated with BCG and those experimentally infected with M. bovis. BCG vaccination induced minimal protection in the present study,

with similar numbers of animals infected with M. bovis in BCG-vaccinated and nonvaccinated groups. Following vaccination with BCG, the animals produced moderate IFN-gamma responses to bovine purified protein derivative (PPDB) but very weak responses to the recombinant antigens. Cattle from both the BCG-vaccinated and nonvaccinated groups which were M. bovis culture positive following challenge produced IFN-gamma responses to PPDB and ESAT-6 which were significantly stronger than those observed in the corresponding M. bovis culture-negative animals. IFN-gamma responses to MPB59, MPB64, and MPB70 were significantly weaker, and these antigens could not discriminate between vaccinated animals which develop disease and the culture-negative animals. The results of the study indicate that of the four antigens tested in the IFN-gamma assay, only ESAT-6 would be suitable for differentiating BCG-vaccinated animals from those infected with bovine ***tuberculosis*** .

L6 ANSWER 31 OF 61 CAPLUS COPYRIGHT 2001 ACS
AN 1998:684968 CAPLUS
DN 129:300060
TI Novel antigens of Mycobacterium ***tuberculosis*** culture filtrates and the genes encoding and their diagnostic and prophylactic use
IN ***Andersen, Peter*** ; Nielsen, Rikke; Rosenkrands, Ida; Weldingh, Karin; Rasmussen, Peter Birk; Oettinger, Thomas; Florio, Walter
PA Statens Serum Institut, Den.
SO PCT Int. Appl., 264 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9844119	A1	19981008	WO 1998-DK132	19980401
W: AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, CZ, DE, DE, DK, DK, EE, EE, ES, FI, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9868204	A1	19981022	AU 1998-68204	19980401
EP 972045	A1	20000119	EP 1998-913536	19980401
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
WO 9924577	A1	19990520	WO 1998-DK438	19981008
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1029053	A1	20000823	EP 1998-947412	19981008
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,				

IE, FI
PRAI DK 1997-376 A 19970402
US 1997-44624 P 19970418
DK 1997-1277 A 19971110
US 1998-70488 P 19980105
WO 1998-DK132 W 19980401
WO 1998-DK438 W 19981008
AB Culture filtrate antigens of Mycobacterium ***tuberculosis*** are characterized and cDNAs encoding them are cloned. Some of the proteins are antigenic and suitable for use in vaccines and in diagnosis of infections, e.g. skin tests. A fusion protein of two of these antigens is a superior immunogen compared to the unfused proteins. Individual antigens from culture filtrates were identified by T cell mapping using T cells from memory immune mice. Genes for individual antigens were then cloned by screening a .lambda.gt11 expression vector with monoclonal antibodies. Manuf. of individual antigens with hexahistidine affinity labels is described.

L6 ANSWER 32 OF 61 USPATFULL
AN 1998:146898 USPATFULL
TI Apparatus and process for electroelution of a gel containing charged macromolecules
IN ***Andersen, Peter*** , Lystrupvej 7, DK-2700 Bronshoj, Denmark
PI US 5840169 19981124
WO 9316788 19930902
AI US 1995-290993 19950313 (8)
WO 1992-DK58 19920225
19950313 PCT 371 date
19950313 PCT 102(e) date
DCD 20110813
DT Utility
EXNAM Primary Examiner: Gorgos, Kathryn L.; Assistant Examiner: Noguerda, Alex
LREP Anderson, Denton L., Farah, David A.Sheldon & Mak, Inc.
CLMN Number of Claims: 53
ECL Exemplary Claim: 32
DRWN 8 Drawing Figure(s); 8 Drawing Page(s)
LN.CNT 462
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A process for electroelution of a gel containing charged macromolecules, such as proteins or polynucleotides, comprising the steps of providing a plurality of adjacent parallel chambers having a trapezoidal cross-section, placing a gel containing the charged macromolecules onto first open sides of the chambers, placing a semipermeable membrane onto second open sides of the chambers, filling the chambers with an elution buffer and applying a voltage difference across the chambers so that charged macromolecules in the gel migrate into the elution buffers in the chambers. Also, an apparatus for electroelution of a gel containing charged macromolecules having, preferably, a plurality of adjacent parallel chambers having a trapezoidal cross-section and vents for removing the product without disassembling the apparatus.

L6 ANSWER 33 OF 61 BIOSIS COPYRIGHT 2001 BIOSIS
AN 1998:237038 BIOSIS
DN PREV199800237038
TI Immunity to mycobacteria with emphasis on ***tuberculosis*** :

Implications for rational design of an effective ***tuberculosis*** vaccine.
AU Kaufmann, Stefan H. E. (1); ***Andersen, Peter***
CS (1) Dep. Immunol., Univ. Ulm, D-89070 Ulm Germany
SO Liew, F. Y. [Editor]; Cox, F. E. G. [Editor]. Chemical Immunology, (1998) Vol. 70, pp. 21-59. Chemical Immunology; Immunology of intracellular parasitism.
Publisher: S. Karger AG P.O. Box, Allschwilerstrasse 10, CH-4009 Basel, Switzerland.
ISSN: 1015-0145. ISBN: 3-8055-6621-2.
DT Book; General Review
LA English

L6 ANSWER 34 OF 61 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 20
AN 1998:393332 BIOSIS
DN PREV199800393332
TI Two-dimensional electrophoresis for analysis of Mycobacterium ***tuberculosis*** culture filtrate and purification and characterization of six novel proteins.
AU Weldingh, Karin; Rosenkrands, Ida; Jacobsen, Susanne; Rasmussen, Peter Birk; Elhay, Martin J.; ***Andersen, Peter (1)***
CS (1) Dep. TB Immunol., Statens Serum Inst., Artillerivej 5, DK-2300 Copenhagen Denmark
SO Infection and Immunity, (Aug., 1998) Vol. 66, No. 8, pp. 3492-3500.
ISSN: 0019-9567.
DT Article
LA English
AB Culture filtrate from Mycobacterium ***tuberculosis*** contains molecules which promote high levels of protective immunity in animal models of subunit vaccination against ***tuberculosis*** . We have used two-dimensional electrophoresis for analysis and purification of six novel M. ***tuberculosis*** culture filtrate proteins (CFPs): CFP17, CFP20, CFP21, CFP22, CFP25, and CFP28. The proteins were tested for recognition by M. ***tuberculosis*** -reactive memory cells from different strains of inbred mice and for their capacity to induce a skin test response in M. ***tuberculosis*** -infected guinea pigs. CFP17, CFP20, CFP21 and CFP25 induced both a high gamma interferon release and a strong delayed-type hypersensitivity response, and CFP21 was broadly recognized by different strains of inbred mice. N-terminal sequences were obtained for the six proteins, and the corresponding genes were identified in the Sanger M. ***tuberculosis*** genome database. In parallel we established a two-dimensional electrophoresis reference may of short-term culture filtrate components and mapped novel proteins as well as already-known CFP.

L6 ANSWER 35 OF 61 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 21
AN 1998:348514 BIOSIS
DN PREV199800348514
TI Delayed-type hypersensitivity responses to ESAT-6 and MPT64 from Mycobacterium ***tuberculosis*** in the guinea pig.
AU Elhay, Martin J.; Oettinger, Thomas; ***Andersen, Peter (1)***
CS (1) Dep. T.B. Immunol., Statens Serum Inst., Artillerivej 5, Copenhagen 2300 Denmark
SO Infection and Immunity, (July, 1998) Vol. 66, No. 7, pp. 3454-3456.
ISSN: 0019-9567.

DT Article
LA English
AB Two antigens from Mycobacterium ***tuberculosis*** , ESAT-6 and MPT64, elicited delayed-type hypersensitivity (DTH) skin responses in outbred guinea pigs infected with M. ***tuberculosis*** by the aerosol and intravenous routes but not those sensitized with M. bovis BCG or M. avium. The DTH epitope of ESAT-6 was mapped to the C terminus. Nonresponders to the individual antigens were found, but all animals responded to a combination of ESAT-6 and MPT64 or their respective minimal target peptides. Correspondingly, these molecules could form the basis of a new skin test for ***tuberculosis*** .

L6 ANSWER 36 OF 61 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 22
AN 1999:28278 BIOSIS
DN PREV199900028278
TI A Mycobacterium ***tuberculosis*** operon encoding ESAT-6 and a novel low-molecular-mass culture filtrate protein (CFP-10.
AU Berthet, Fancois-Xavier (1); Rasmusse, Peter Birk; Rosenkrands, Ida; ***Andersen, Peter*** ; Gicquel, Brigitte
CS (1) Unite Geneitque Mycobacteriene, Inst. Pasteur, 25 rue Dr Roux, 75724 Paris Cedex 15 France
SO Microbiology (Reading), (Nov., 1998) Vol. 144, No. 11, pp. 3195-3203. ISSN: 1350-0872.
DT Article
LA English
AB The early secreted antigenic target 6 kDa protein (ESAT-6) is a potent T-cell protein antigen synthesized by Mycobacterium ***tuberculosis*** . Its corresponding gene (esat-6) is located in RD1, a 10 kb DNA region deleted in the attenuated ***tuberculosis*** vaccine strain Mycobacterium bovis BCG. The promoter region of M. ***tuberculosis*** esat-6 was cloned and characterized. A new gene, designated lhp and cotranscribed with esat-6, was identified. Moreover, computer searches in the M. ***tuberculosis*** genome identified 13 genes related to the lhp/esat-6 operon, defining a novel gene family. The transcription initiation sites of the lhp/esat-6 operon were mapped using M. ***tuberculosis*** RNA. The corresponding promoter signals were not recognized in Mycobacterium smegmatis, in which transcription of lhp/esat-6 is initiated at different locations. The M. ***tuberculosis*** lhp gene product was identified as CFP-10, a low-molecular-mass protein found in the short-term culture filtrate. These results show that the genes encoding CFP-10 and ESAT-6 are transcribed together in M. ***tuberculosis*** and that both code for small exported proteins.

L6 ANSWER 37 OF 61 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 23
AN 1998:304925 BIOSIS
DN PREV199800304925
TI Identification and characterization of a 29-kilodalton protein from Mycobacterium ***tuberculosis*** culture filtrate recognized by mouse memory effector cells.
AU Rosenkrands, Ida; Rasmussen, Peter Birk; Carnio, Markus; Jacobsen, Susanne; Theisen, Michael; ***Andersen, Peter (1)***
CS (1) Dep. TB Immunol., Statens Serum Inst., 5 Artillerivej, DK-2300 Copenhagen S Denmark
SO Infection and Immunity, (June, 1998) Vol. 66, No. 6, pp. 2728-2735.

ISSN: 0019-9567.
DT Article
LA English
AB Culture filtrate proteins from Mycobacterium ***tuberculosis*** induce protective immunity in various animal models of ***tuberculosis*** . Two molecular mass regions (6 to 10 kDa and 24 to 36 kDa) of short-term culture filtrate are preferentially recognized by Th1 cells in animal models as well as by patients with minimal disease. In the present study, the 24- to 36-kDa region has been studied, and the T-cell reactivity has been mapped in detail. Monoclonal antibodies were generated, and one monoclonal antibody, HYB 71-2, with reactivity against a 29-kDa antigen located in the highly reactive region below the antigen 85 complex was selected. The 29-kDa antigen (CFP29) was purified from M. ***tuberculosis*** short-term culture filtrate by thiophilic adsorption chromatography, anion-exchange chromatography, and gel filtration. In its native form, CFP29 forms a polymer with a high molecular mass. CFP29 was mapped in two-dimensional electrophoresis gels as three distinct spots just below the antigen 85 complex component MPT59. CFP29 is present in both culture filtrate and the membrane fraction from M. ***tuberculosis*** , suggesting that this antigen is released from the envelope to culture filtrate during growth. Determination of the N-terminal amino acid sequence allowed cloning and sequencing of the cfp29 gene. The nucleotide sequence showed 62% identity to the bacteriocin Linocin from Brevibacterium linens. Purified recombinant histidine-tagged CFP29 and native CFP29 had similar T-cell stimulatory properties, and they both elicited the release of high levels of gamma interferon from mouse memory effector cells isolated during the recall of protective immunity to ***tuberculosis*** . Interspecies analysis by immunoblotting and PCR demonstrated that CFP29 is widely distributed in mycobacterial species.

L6 ANSWER 38 OF 61 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 24
AN 1998:120633 BIOSIS
DN PREV199800120633
TI B-cell epitopes and quantification of the ESAT-6 protein of Mycobacterium ***tuberculosis*** .
AU Harboe, Morten (1); Malin, Adam S.; Dockrell, Hazel S.; Wiker, Harald Gotten; Ulvund, Gunni; Holm, Arne; Jorgensen, Mikala Clok; ***Andersen,*** *** Peter***
CS (1) Inst. Immunol. Rheumatol., Univ. Oslo, Fr. Qvams gate 1, N-0172 Oslo Norway
SO Infection and Immunity, (Feb., 1998) Vol. 66, No. 2, pp. 717-723. ISSN: 0019-9567.
DT Article
LA English
AB ESAT-6 is an important T-cell antigen recognized by protective T cells in animal models of infection with Mycobacterium ***tuberculosis*** . In an enzyme-linked immunosorbent assay (ELISA) with overlapping peptides spanning the sequence of ESAT-6, monoclonal antibody HYB76-8 reacted with two peptides in the N-terminal region of the molecule. Assays with synthetic truncated peptides allowed a precise mapping of the epitope to the residues EQQWNFAGIEAAA at positions 3 to 15. Hydrophilicity plots revealed one hydrophilic area at the N terminus and two additional areas further along the polypeptide chain. Antipeptide antibodies were generated by immunization with synthetic 8-mer peptides corresponding to these two regions coupled to keyhole limpet hemocyanin. Prolonged immunization with

a 23-mer peptide (positions 40 to 62) resulted in the formation of antibodies reacting with the peptide as well as native ESAT-6. A double-antibody ELISA was then developed with monoclonal antibody HYB76-8 as a capture antibody, antigen for testing in the second layer, and antipeptide antibody in the third layer. The assay was suitable for quantification of ESAT-6 in M. ***tuberculosis*** antigen preparations, showing no reactivity with M. bovis BCG Tokyo culture fluid, used as a negative control, or with MPT64 or antigen 85B, previously shown to cross-react with HYB76-8. This capture ELISA permitted the identification of ESAT-6 expression from vaccinia virus constructs containing the esat-6 gene; this expression could not be identified by standard immunoblotting.

L6 ANSWER 39 OF 61 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 25
AN 1998:93855 BIOSIS
DN PREV199800093855
TI Human cytolytic and interferon gamma-secreting CD8+ T lymphocytes specific for Mycobacterium ***tuberculosis*** .
AU Lalvani, Ajit; Brookes, Roger (1); Wilkinson, Robert J.; Malin, Adam S.; Pathan, Ansar A.; ***Andersen, Peter*** ; Dockrell, Hazel; Pasvol, Geoffrey; Hill, Adrian V. S.
CS (1) Mol. Immunol. Group, Inst. Mol. Med., Nuffield Dep. Clin. Med., Univ. Oxford, John Radcliffe Hosp., Oxford OX3 9DU UK
SO Proceedings of the National Academy of Sciences of the United States of America, (Jan. 6, 1998) Vol. 95, No. 1, pp. 270-275.
ISSN: 0027-8424.
DT Article
LA English
AB Protective immunity to Mycobacterium ***tuberculosis*** is poorly understood, but mounting evidence, at least in animal models, implicates major histocompatibility complex class I-restricted CD8+ T cells as an essential component. By using a highly sensitive assay for single cell interferon y release, we screened an array of M. ***tuberculosis*** antigen-derived peptides congruent with HLA class I allele-specific motifs. We identified CD8+ T cells specific for epitopes in the early secretory antigenic target 6 during active ***tuberculosis*** , after clinical recovery and in healthy contacts. Unrestimulated cells exhibited peptide-specific interferon gamma secretion, whereas lines or clones recognized endogenously processed antigen and showed cytolytic activity. These results provide direct evidence for the involvement of CD8+ cytotoxic T lymphocytes in host defense against M. ***tuberculosis*** in humans and support current attempts to generate protective cytotoxic T lymphocyte responses against M. ***tuberculosis*** by vaccination.

L6 ANSWER 40 OF 61 CAPLUS COPYRIGHT 2001 ACS
AN 1998:320603 CAPLUS
DN 129:121218
TI Immunity to mycobacteria with emphasis on ***tuberculosis*** : implications for rational design of an effective ***tuberculosis*** vaccine
AU Kaufmann, Stefan H. E.; ***Andersen, Peter***
CS Department of Immunology, University of Ulm, Ulm, D-89070, Germany
SO Chem. Immunol. (1998), 70(Immunology of Intracellular Parasitism), 21-59
CODEN: CHMIEP; ISSN: 1015-0145
PB S. Karger AG

DT Journal; General Review
LA English
AB A review with 235 refs. Discussed are: mycobacterial diseases; T cells as central mediators of protection; mycobacterial localization and antigen presentation; CD4 T lymphocytes; CD8 T cells; .gamma..delta. T cells; DN.alpha..beta. T cells; cytokines; cytolytic T lymphocyte responses; T cells mediating immunol. memory; mycobacterial antigens; mycobacterial antigens recognized by T cells; extracellular vs. somatic antigens - early vs. late antigens; the design of novel vaccines against ***tuberculosis*** ; subunit vaccines; recombinant carriers; other carriers; attenuated mycobacterial strains; DNA vaccines; and testing of exptl. vaccines in animal models.

L6 ANSWER 41 OF 61 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 26
AN 1997:345563 BIOSIS
DN PREV199799644766
TI Predominant recognition of the ESAT-6 protein in the first phase of infection with Mycobacterium bovis in cattle.
AU Pollock, John M.; ***Andersen, Peter (1)***
CS (1) Dep. TB Immunol., Statens Serum Inst, 5 Artillerivej, DK-2300 Copenhagen S Denmark
SO Infection and Immunity, (1997) Vol. 65, No. 7, pp. 2587-2592. ISSN: 0019-9567.
DT Article
LA English
AB ***Tuberculosis*** continues to be a worldwide health problem for both humans and animals. The development of improved vaccines and diagnostic tests requires detailed understanding of the immune responses generated and the antigens recognized during the disease. This study examined the T-cell response which develops in cattle experimentally infected with Mycobacterium bovis. The first significant T-cell response was found 3 weeks after the onset of infection and was characterized by a pronounced gamma interferon (IFN-gamma) response from peripheral blood mononuclear cells directed to antigens in culture filtrates. Short-term culture filtrate (ST-CF) was separated into molecular mass fractions and screened for recognition by T cells from experimentally infected and field cases of bovine ***tuberculosis*** . Cattle in the early stages of experimental infection were characterized by strong IFN-gamma responses directed predominantly toward the lowest-mass (lt 10-kDa) fraction of ST-CF, but cattle in later stages of experimental infection (16 weeks postinfection) exhibited a broader recognition of antigens of various molecular masses. Field cases of bovine ***tuberculosis*** , in comparison, preferentially recognized low-mass antigens, characteristic of animals in the early stages of infection. The major T-cell target for this dominant IFN-gamma response was found to be the secreted antigen ESAT-6. This antigen was recognized strongly by the majority of field cases of bovine ***tuberculosis*** tested. As ESAT-6 is unique to pathogenic mycobacterial species, our study suggests that ESAT-6 is an antigen with major potential for vaccination against and specific diagnosis of bovine ***tuberculosis*** .

L6 ANSWER 42 OF 61 CAPLUS COPYRIGHT 2001 ACS
AN 1997:120149 CAPLUS
DN 126:210703
TI Human T cell responses induced by vaccination with Mycobacterium bovis

bacillus Calmette-Guerin
AU Ravn, Pernille; Boesen, Henriette; Pedersen, Bente Klarlund; ***Andersen, Peter***
CS Tuberculosis Research Unit, Statens Serum Institut, Copenhagen, Den.
SO J. Immunol. (1997), 158(4), 1949-1955
CODEN: JOIMA3; ISSN: 0022-1767
PB American Association of Immunologists
DT Journal
LA English
AB Many aspects of the widely used bacillus Calmette-Guerin (BCG) vaccine against ***tuberculosis*** are still the subject of controversy. There is a huge variation in efficacy from one clin. trial to another and no relation between vaccine-induced skin test conversion and subsequent protection. We have studied in vitro cell-mediated immune responses primed by BCG vaccination in 22 healthy Danish donors with different levels of in vitro purified protein deriv. (PPD) reactivity before vaccination. The study demonstrated a markedly different development of reactivity to mycobacterial Ags depending on the prevaccination sensitivity to PPD. Previously sensitized donors mounted a potent and highly accelerated recall response within the first week of BCG vaccination. Nonsensitized donors, in contrast, exhibited a gradually increasing responsiveness to mycobacterial Ags, reaching maximal levels between day 56 and 365 postvaccination. The recognition of different classes of Ags were induced in a stepwise manner: culture filtrate Ags were recognized 1 wk postvaccination followed by cell wall, membrane, and the cytosolic Ag fraction. The T cell response primed by BCG vaccination was characterized as a CD4 response with a Th1-like cytokine pattern and substantial levels of Ag-specific cytotoxicity. The specificity of the T cell response generated was broad and directed to a range of culture filtrate Ag fractions. The study shows that BCG vaccination of previously nonsensitized donors can provide important data on potentially protective immune responses in humans and suggest a careful evaluation of prevaccination sensitivity when investigating vaccine-induced immunity.

L6 ANSWER 43 OF 61 BIOSIS COPYRIGHT 2001 BIOSIS
AN 1997:251430 BIOSIS
DN PREV199799550633
TI The potential of the ESAT-6 antigen secreted by virulent mycobacteria for specific diagnosis of ***tuberculosis*** .
AU Pollock, John M.; ***Andersen, Peter (1)***
CS (1) TB-Res. Unit, Statens Seruminst., Artillerivej 5, DK-2300, Copenhagen S Denmark
SO Journal of Infectious Diseases, (1997) Vol. 175, No. 5, pp. 1251-1254. ISSN: 0022-1899.
DT Article
LA English
AB ***Tuberculosis*** (TB) remains a global health problem in humans and animals, and improved diagnostic methods are needed urgently. This study examined the potential of an interferon-gamma blood test based on a recently identified low-molecular-mass secreted protein antigen, ESAT-6, for early detection of bovine TB. It was found that field cases of bovine TB and experimentally infected cattle exhibited strong in vitro interferon-gamma responses directed toward this antigen. Of importance, ESAT-6 reactivity was found to discriminate between cattle infected with TB and cattle sensitized by environmental mycobacteria, and the gene

encoding this molecule was demonstrated to be absent from gt 90% of the nontuberculous mycobacterial strains isolated from healthy sensitized cattle. These results demonstrate the feasibility of using single defined antigens for the highly specific diagnosis of TB.

L6 ANSWER 44 OF 61 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 27
AN 1997:111200 BIOSIS
DN PREV199799410403
TI Adjuvant modulation of immune responses to ***tuberculosis*** subunit vaccines.
AU Lindblad, Erik B.; Elhay, Martin J.; Silva, Regina; Appelberg, Rui; ***Andersen, Peter (1)***
CS (1) TB Res. Unit, Bacterial Vaccine Dep., Statens Seruminstitut, Artillerivej 5, 2300 Copenhagen S. Denmark
SO Infection and Immunity, (1997) Vol. 65, No. 2, pp. 623-629. ISSN: 0019-9567.
DT Article
LA English
AB Mice were immunized with experimental subunit vaccines based on secreted antigens from Mycobacterium ***tuberculosis*** in a series of adjuvants, comprising incomplete Freund's adjuvant (IFA), dimethyl dioctadecyl ammoniumbromide (DDA), RIBI adjuvant, Quil-A saponin, and aluminum hydroxide. Immune responses induced by these vaccines were characterized by in vitro culture of primed cells, PCR analysis for cytokine mRNA, detection of specific immunoglobulin G isotypes induced, and monitoring of protective immunity to ***tuberculosis*** (TB). The study demonstrated marked differences in the immune responses induced by the different adjuvants and identified both IFA and DDA as efficient adjuvants for a TB subunit vaccine. Aluminum hydroxide, on the other hand, induced a Th2 response which increased the susceptibility of the animals to a subsequent TB challenge. DDA was further coadjuvanted with either the Th1-stimulating polymer poly(I-C) or the cytokines gamma interferon, interleukin 2 (IL-2), and IL-12. The addition of IL-12 was found to amplify a Th1 response in a dose-dependent manner and promoted a protective immune response against a virulent challenge. However, if the initial priming in the presence of IL-12 was followed by two booster injections of vaccine without IL-12, no improvement in long-term efficacy was found. This demonstrates the efficacy of DDA to promote an efficient immune response and suggests that IL-12 may accelerate this development, but not change the final outcome of a full vaccination regime.

L6 ANSWER 45 OF 61 BIOSIS COPYRIGHT 2001 BIOSIS
AN 1998:136294 BIOSIS
DN PREV199800136294
TI Immunological requirements for a subunit vaccine against ***tuberculosis*** .
AU Elhay, Martin J.; ***Andersen, Peter (1)***
CS (1) Dep. TB Immunol., Statens Serum Institut, Artillerivej 5, Copenhagen 2300 S Denmark
SO Immunology and Cell Biology, (Dec., 1997) Vol. 75, No. 6, pp. 595-603. ISSN: 0818-9641.
DT General Review
LA English
AB ***Tuberculosis*** remains one of the most important threats to world health. Current vaccination and prevention strategies are inadequate and

there is an urgent need for a new vaccine. The current vaccine bacille Calmette-Guerin (BCG), is unable to protect against re-activation of disease in later life and its efficacy varies tremendously in different human populations. An ideal replacement would be a non-living subunit vaccine that could impart protective efficacy greater than BCG but without its drawbacks. Before such a goal is achieved, however, there are many parameters that need to be examined in experimental systems. Such studies have revealed that apart from the selection of immunologically relevant antigens, dosage of antigen and type of adjuvant need to be chosen carefully. These parameters need to be examined in the context of the complex biology of the disease and, despite recent progress in defining host/pathogen interactions, experimental vaccines tested so far have fallen short of the protective efficacy of BCG. A coordinated approach, stimulating the various facets of cell-mediated immunity will probably be essential for development of protective immunity through subunit vaccination.

L6 ANSWER 46 OF 61 CAPLUS COPYRIGHT 2001 ACS
AN 1996:632476 CAPLUS
DN 125:325659
TI Key epitopes on the ESAT-6 antigen recognized in mice during the recall of protective immunity to Mycobacterium ***tuberculosis***
AU Brandt, Lise; Oettinger, Thomas; Holm, Arne; Andersen, Aase B.; ***Andersen, Peter***
CS Bacterial Vaccine and Mycobacteria Dep., Royal Veterinary and Agricultural Univ., Copenhagen, Den.
SO J. Immunol. (1996), 157(8), 3527-3533
CODEN: JOIMA3; ISSN: 0022-1767
DT Journal
LA English
AB The recall of long-lived immunity in a mouse model of ***tuberculosis*** (TB) is defined as an accelerated accumulation of reactive T cells in the target organs. The authors have recently identified antigen (Ag) 85B and a 6-kDa early secretory antigenic target, designated ESAT-6, as key antigenic targets recognized by these cells. Here, preferential recognition of the ESAT-6 Ag during the recall of immunity was shared by 5 of 6 genetically different strains of mice. Overlapping peptides spanning the sequence of ESAT-6 were used to map 2 T cell epitopes on this mol. One epitope recognized in the context of H-2b,d was located in the N-terminal part of the mol., whereas an epitope recognized in the context of H-2a,k covered amino acids 51-60. Shorter versions of the N-terminal epitope allowed the precise definition of a 13-amino acid core sequence recognized in the context of H-2b. The peptide covering the N-terminal epitope was immunogenic, and a T cell response with the same fine specificity as that induced during TB infection was generated by immunization with the peptide in IFA. In the C57BL/6j strain, this single epitope was recognized by an exceedingly high frequency of splenic T cells (.apprx.1:1000), representing 25-35% of the total culture filtrate-reactive T cells recruited to the site of infection during the first phase of the recall response. These findings emphasize the relevance of this Ag in the immune response to TB and suggest that immunol. recognition in the first phase of infection is a highly restricted event dominated by a limited no. of T cell clones.

L6 ANSWER 47 OF 61 BIOSIS COPYRIGHT 2001 BIOSIS

AN 1996:475250 BIOSIS
DN PREV199699204806
TI European Commission COST/STD initiative: Report of the Expert Panel IX: Vaccines against ***Tuberculosis*** .
AU Harboe, Morten (1); ***Andersen, Peter*** ; Colston, Michael J.; Gicquel, Brigitte; Hermans, Peter W. M.; Ivanyi, Juraj; Kaufman, Stefan H. E.
CS (1) Inst. Immunol. Rheumatol., Univ. Oslo, Oslo N-0172 Norway
SO Vaccine, (1996) Vol. 14, No. 7, pp. 701-716.
ISSN: 0264-410X.
DT Article
LA English

L6 ANSWER 48 OF 61 BIOSIS COPYRIGHT 2001 BIOSIS
AN 1997:102941 BIOSIS
DN PREV199799402144
TI ESAT-6 as a diagnostic reagent with increased specificity for bovine ***tuberculosis*** .
AU Pollock, John M. (1); ***Andersen, Peter***
CS (1) Vet. Sci. Div., Stormont, Belfast UK
SO Immunology, (1996) Vol. 89, No. SUPPL. 1, pp. 63.
Meeting Info.: Joint Congress of the British Society for Immunology and the Biochemical Society Harrogate, England, UK December 10-13, 1996
ISSN: 0019-2805.
DT Conference; Abstract; Conference
LA English

L6 ANSWER 49 OF 61 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 28
AN 1996:76919 BIOSIS
DN PREV199698649054
TI Evidence for occurrence of the ESAT-6 protein in Mycobacterium ***tuberculosis*** and virulent Mycobacterium bovis and for its absence in Mycobacterium bovis BCG.
AU Harboe, Morten (1); Oettinger, Thomas; Wiker, Harald Gotten; Rosenkrands, Ida; ***Andersen, Peter***
CS (1) Inst. Immunol. Rheumatol., Univ. Oslo, N-0172 Oslo Norway
SO Infection and Immunity, (1996) Vol. 64, No. 1, pp. 16-22.
ISSN: 0019-9567.
DT Article
LA English
AB ESAT-6 is a secreted protein present in the short-term culture filtrate of Mycobacterium ***tuberculosis*** after growth on a synthetic Sauton medium. ESAT-6 has recently been demonstrated to induce strong T-cell responses in a mouse model of memory immunity after infection with M. ***tuberculosis*** . In Western blotting (immunoblotting), the monoclonal antibody HYB76-8. reacting with ESAT-6, gave a 6-kDa band in culture filtrates from M. ***tuberculosis*** and virulent Mycobacterium bovis. A distinct band in the 24-kDa region was observed in filtrates from four of eight substrains of M. bovis BCG that produced high levels of MPB64, while no band occurred in the 6-kDa region with any of these BCG substrains. Southern blotting and PCR experiments with genomic mycobacterial DNA showed the presence of the esat-6 gene in reference strains and clinical isolates of V. ***tuberculosis*** as well as in virulent M. bovis. The esat-6 gene could not be demonstrated in any of the eight substrains of M. bovis BCG tested by these techniques. Two gene

deletions that distinguish M. bovis BCG from virulently M. bovis have thus now been demonstrated. Deletion of mpb64 affects four of the eight substrains tested; deletion of esat-6 affects all of them. The reaction of HYB76-8 at 26 kDa with four of the BCG substrains was demonstrated to result from cross-reactivity with MPB64. HYB76-8 was also shown to cross-react with the A, B, and C components of the antigen 85 complex and MPT51.

L6 ANSWER 50 OF 61 CAPLUS COPYRIGHT 2001 ACS
AN 1995:501322 CAPLUS
DN 122:237772
TI Low-molecular-weight proteins released by mycobacteria, their manufacture with recombinant cells, and their use in diagnosis and in ***tuberculosis*** vaccines
IN ***Andersen, Peter*** ; Andersen, Aase Bengaard; Hasloev, Kaare; Soerensen, Anne Lund
PA Statens Serumsinstitut, Den.
SO PCT Int. Appl., 100 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9501441	A1	19950112	WO 1994-DK273	19940701
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, CZ, DE, DE, DK, DK, ES, FI, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LU, LV, MD, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, SK, TJ, TT, UA				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2165949	AA	19950112	CA 1994-2165949	19940701
AU 9470688	A1	19950124	AU 1994-70688	19940701
AU 682879	B2	19971023		
EP 706571	A1	19960417	EP 1994-919574	19940701
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
US 5955077	A	19990921	US 1995-465640	19950605

PRAI DK 1993-798 19930702
US 1993-123182 19930920
WO 1994-DK273 19940701

AB The invention relates to a secreted antigenes from mycobacteria capable of evoking early (within 4 days) immunol. responses from T-helper cells in the form of .gamma.-interferon release in memory immune animals after rechallenge infection with mycobacteria of the ***tuberculosis*** complex. The antigens are present in short term culture filtrates from cultured mycobacteria belonging to the ***tuberculosis*** complex. One of these antigens, a polypeptide with an apparent mol. wt. of 6 kDa, has been identified, and the DNA encoding the polypeptide has been cloned and sequenced. Also disclosed are methods of immunizing animals/humans and methods of diagnosing ***tuberculosis*** .

L6 ANSWER 51 OF 61 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 29
AN 1995:222413 BIOSIS
DN PREV199598236713
TI Recall of long-lived immunity to Mycobacterium ***tuberculosis***

infection in mice.
AU ***Andersen, Peter (1)*** ; Andersen, Ase B.; Sorensen, Anne L.; Nagai, Sadamu
CS (1) Bacterial Vaccine Dep., Statens Seruminstitut, Artillerivej 5, 2300 Copenhagen S Denmark
SO Journal of Immunology, (1995) Vol. 154, No. 7, pp. 3359-3372. ISSN: 0022-1767.
DT Article
LA English
AB Our study investigates the recall of immunity in the mouse model of memory immunity to ***tuberculosis*** infection. The results provide evidence that recall of immunity is expressed as an accelerated accumulation of potent effector cells in the infected target organs. These effector cells were recruited from the resting pool of memory cells and were immediately triggered to exert their effector functions, leading to a massive release of Th1 cytokines detectable both in splenic extracts and in the serum within the first 24 h of infection. During a primary infection, in contrast, a 14-day delay was observed before significant cytokine levels were reached. After the initial effector phase, the cells blasted and entered into clonal expansion, resulting in a rapid increase in the total number of CD4 CD45RB-low cells in the spleen. The recall of memory immunity was highly efficient and controlled an infectious challenge within the first week. The molecules recognized by the memory effector subset were the proteins secreted from Mycobacterium ***tuberculosis*** during growth. By separating the CD4 population into CD45RB-high and CD45RB-low subsets, the memory effector cells were demonstrated to reside predominantly in the activated population of CD45RB-low CD44-high L-FA-1-high L-selectin-low cells. The key antigenic targets recognized by these cells were identified as Ag85B and a secreted 6-kDa protein (ESAT-6) that elicited the release of exceedingly high levels of IFN-gamma. ESAT-6 was biochemically purified, characterized, and the gene encoding the protein was cloned.

L6 ANSWER 52 OF 61 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 30
AN 1995:272492 BIOSIS
DN PREV199598286792
TI Purification and Characterization of a Low-Molecular-Mass T-Cell Antigen Secreted by Mycobacterium ***tuberculosis*** .
AU Sorensen, Anne L.; Nagai, Sadamu; Houen, Gunnar; ***Andersen, Peter*** ; Andersen, Ase B. (1)
CS (1) Mycobacteria Dep., Statens Seruminstitut, Artillerivej 5, DK-2300 Copenhagen S Denmark
SO Infection and Immunity, (1995) Vol. 63, No. 5, pp. 1710-1717. ISSN: 0019-9567.
DT Article
LA English
AB A novel immunogenic antigen, the 6-kDa early secretory antigenic target (ESAT-6), from short-term culture filtrates of Mycobacterium ***tuberculosis*** was purified by hydrophobic interaction chromatography and anion-exchange chromatography by use of fast protein liquid chromatography. The antigen focused at two different pIs of 4.0 and 4.5 during isoelectric focusing, and each of these components separated into three spots ranging from 4 to 6 kDa during two-dimensional sodium dodecyl sulfate-polyacrylamide gel electrophoresis. The apparent differences in molecular masses or pIs of these isoforms were not due to

posttranslational glycosylation. The molecular weight of the purified native protein was determined by applying gel filtration and nondenaturing polyacrylamide gel electrophoresis and found to be 24 kDa. ESAT-6 is recognized by the murine monoclonal antibody HYB 76-8, which was used to screen a recombinant lambda-gt11 M. ***tuberculosis*** DNA library. A phage expressing a gene product recognized by HYB 76-8 was isolated, and a 1.7-kbp fragment of the mycobacterial DNA insert was sequenced. The structural gene of ESAT-6 was identified as the sequence encoding a polypeptide of 95 amino acids. The N terminus of the deduced sequence could be aligned with the 10 amino-terminal amino acids derived from sequence analyses of the native protein. N-terminal sequence analysis showed that the purified antigen was essentially free from contaminants, and the amino acid analysis of the antigen was in good agreement with the DNA sequence-deduced amino acid composition. Thus, the heterogeneities observed in the pI and molecular weight of the purified antigen do not derive from contaminating proteins but are most likely due to heterogeneity of the antigen itself. Native and recombinant ESAT-6 are immunologically active in that both elicited a high release of gamma interferon from T cells isolated from memory-immune mice challenged with M. ***tuberculosis*** . Analyses of subcellular fractions of M. ***tuberculosis*** showed the presence of ESAT-6 in cytosol- and cell wall-containing fractions. Interspecies analyses showed the presence of ESAT-6 in filtrates from M. ***tuberculosis*** complex species. Among filtrates from mycobacteria not belonging to the M. ***tuberculosis*** complex, reactivity was observed in Mycobacterium kansasii, Mycobacterium szulgai, and Mycobacterium marinum.

L6 ANSWER 53 OF 61 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 31
AN 1995:221142 BIOSIS
DN PREV199598235442
TI Human T-cell responses to secreted antigen fractions of Mycobacterium ***tuberculosis*** .
AU Boesen, Henriette; Jensen, Birgitte Nybo; Wilcke, Torgny; ***Andersen,*** *** Peter (1)***
CS (1) Bacterial Vaccine Dep., Statens Seruminstitut, Artillerivej 5, 2300 Copenhagen Denmark
SO Infection and Immunity, (1995) Vol. 63, No. 4, pp. 1491-1497. ISSN: 0019-9567.
DT Article
LA English
AB The T-cell response of human donors to secreted antigen fractions of Mycobacterium ***tuberculosis*** was investigated. The donors were divided into five groups: active pulmonary ***tuberculosis*** (TB) patients with minimal and with advanced disease, Mycobacterium bovis BCG-vaccinated donors with and without contact with TB patients, and nonvaccinated individuals. We found that patients with active minimal TB responded powerfully to secreted antigens contained in a short-term culture filtrate. The response to secreted antigens was mediated by CD4+ Th-1-like lymphocytes, and the gamma interferon release by these cells was markedly higher in patients with active minimal TB than in healthy BCG-vaccinated donors. Patients with active advanced disease exhibited depressed responses to all preparations tested. The specificity of the response to secreted antigens was investigated by stimulating lymphocytes with narrow-molecular-mass fractions of short-term culture filtrate obtained by the multielution technique. Considerable heterogeneity was

found within the donor groups. Patients with active minimal TB recognized multiple secreted targets, but interestingly, six of eight patients demonstrated a predominant recognition of a low-mass (lt 10-kDa) protein fraction which induced high levels of gamma interferon release in vitro. Only a few of 12 previously characterized secreted antigens were recognized by T cells isolated from TB patients, suggesting the existence of a number of as yet undefined antigenic targets among secreted antigens.

L6 ANSWER 54 OF 61 BIOSIS COPYRIGHT 2001 BIOSIS
AN 1995:147890 BIOSIS
DN PREV199598162190
TI Secreted antigens and protective immunity to ***tuberculosis*** .
AU ***Andersen, Peter***
CS Statens Seruminst., Copenhagen S Denmark
SO Journal of Cellular Biochemistry Supplement, (1995) Vol. 0, No. 19B, pp. 56.
Meeting Info.: Keystone Symposium on Molecular Mechanisms in Tuberculosis Tamarron, Colorado, USA February 19-25, 1995
ISSN: 0733-1959.
DT Conference
LA English

L6 ANSWER 55 OF 61 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 32
AN 1994:301148 BIOSIS
DN PREV199497314148
TI Effective vaccination of mice against Mycobacterium ***tuberculosis*** infection with a soluble mixture of secreted mycobacterial proteins.
AU ***Andersen, Peter***
CS Bacterial Vaccine Dep., Statens Seruminstitut, 5 Artillerivej, DK-2300 Copenhagen S Denmark
SO Infection and Immunity, (1994) Vol. 62, No. 6, pp. 2536-2544.
ISSN: 0019-9567.
DT Article
LA English
AB An experimental vaccine that was based on secreted proteins of Mycobacterium ***tuberculosis*** was investigated in a mouse model of ***tuberculosis*** . I used a short-term culture filtrate (ST-CF) containing proteins secreted from actively replicating bacteria grown under defined culture conditions. The immunogenicity of the ST-CF was investigated in combination with different adjuvants, and peak proliferative responses were observed when ST-CF was administered with the surface-active agent dimethyldioctadecylammonium chloride. The immunity induced by this vaccine was dose dependent, and, in the optimal concentration, the vaccine induced a potent T-helper 1 response which efficiently protected the animals against a subsequent challenge with virulent M. ***tuberculosis*** . Antigenic tar-gets for the T cells generated were mapped by employing narrow-molecular-weight fractions of ST-CF. The experimental vaccine primed a broadly defined T-cell repertoire directed to multiple secreted antigens present in ST-CF. A vaccination with viable Mycobacterium bovis bacillus Calmette-Guerin (BCG), in contrast, induced a restricted T-cell reactivity directed to two secreted protein fractions with molecular masses of 5 to 12 and 25 to 35 kDa. The protective efficacy of the ST-CF vaccine was compared with that of a BCG standard vaccine, and both induced a highly significant protection of equal magnitude. The vaccination with ST-CF gave rise to a population of

long-lived CD4 cells which could be isolated 22 weeks after the vaccination and could adoptively transfer acquired resistance to T-cell-deficient recipients. My results confirm the hypothesis that M. ***tuberculosis*** cells release protective antigens during growth. The high efficacy of a subunit vaccine observed in the present study is discussed as a possible alternative to a live recombinant vaccine carrier.

L6 ANSWER 56 OF 61 BIOSIS COPYRIGHT 2001 BIOSIS
AN 1995:64037 BIOSIS
DN PREV199598078337
TI The T cell response to secreted antigens of Mycobacterium ***tuberculosis*** .
AU ***Andersen, Peter***
CS Statens Seruminst. 5, Artillerivej, DK-2300 Copenhagen S Denmark
SO Immunobiology, (1994) Vol. 191, No. 4-5, pp. 537-547.
ISSN: 0171-2985.
DT Article
LA English
AB Recent information from several laboratories points to proteins secreted from live Mycobacterium ***tuberculosis*** as being involved in protective immunity. We have studied protein release from M. ***tuberculosis*** during growth and have defined 3 different groups of proteins: excreted proteins, secreted proteins of the outer cell wall and cytoplasmic proteins released at late culture timepoints. These findings have lead to the definition of a short-term culture filtrate (ST-CF) enriched in excreted/secreted proteins and with a minimal content of autolytic products. ST-CF was tested as antigen in experimental vaccines against ***tuberculosis*** . A vaccine based on the adjuvant dimethyldioctadecylammonium chloride (DDA) was constructed and demonstrated to induce a potent cell mediated immune response of the Th-1 type. The vaccine was tested in parallel with a BCG standard vaccine and both vaccines induced a highly significant protection of the same magnitude. Molecules within the Ag85 complex and a 6-kDA secreted protein were mapped as the major antigenic targets for long-lived T cells involved in protective immunity against M. ***tuberculosis*** .

L6 ANSWER 57 OF 61 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 33
AN 1993:373799 BIOSIS
DN PREV199345045224
TI T cell response to Mycobacterium ***tuberculosis*** .
AU Orme, Ian M.; ***Andersen, Peter*** ; Boom, W. Henry
CS Dep. Microbiol., Colordo State Univ., Fort Collins, CO 80523 USA
SO Journal of Infectious Diseases, (1993) Vol. 167, No. 6, pp. 1481-1497.
ISSN: 0022-1899.
DT General Review
LA English

L6 ANSWER 58 OF 61 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 34
AN 1993:207892 BIOSIS
DN PREV199395109117
TI Specificity of a protective memory immune response against Mycobacterium ***tuberculosis*** .
AU ***Andersen, Peter (1)*** ; Heron, Iver
CS (1) Bacterial Vaccine Dep., Statens Seruminstitut, Artillerivej 5, DK-2300 Copenhagen S Denmark

SO Infection and Immunity, (1993) Vol. 61, No. 3, pp. 844-851.
ISSN: 0019-9567.
DT Article
LA English
AB We have investigated the memory T-cell immune response to Mycobacterium ***tuberculosis*** infection. C57BL/6J mice infected with M. ***tuberculosis*** were found to generate long-lived memory immunity which provided a heightened state of acquired resistant to a secondary infection. The T-cell response of memory immune mice was directed to all parts of the bacilli, i.e., both secreted and somatic proteins. Major parts of the memory T-cell repertoire were maintained in a highly responsive state by cross-reactive restimulation with antigens present in the normal microbiological environment of the animals. A resting non-cross-reactive part of the memory repertoire was restimulated early during a secondary infection to expand and produce large amounts of gamma interferon. The molecular target of these T cells was identified as a secreted mycobacterial protein with a molecular mass of 3 to 9 kDa.

L6 ANSWER 59 OF 61 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 35
AN 1993:320391 BIOSIS
DN PREV199396028741
TI Simultaneous electroelution of whole SDS-polyacrylamide gels for the direct cellular analysis of complex protein mixtures.
AU ***Andersen, Peter (1)*** ; Heron, Iver
CS (1) Statens Seruminstitute, Bacterial Vaccine Dep., 5 Artillerivej, DK-2300 Copenhagen S Denmark
SO Journal of Immunological Methods, (1993) Vol. 161, No. 1, pp. 29-39.
ISSN: 0022-1759.
DT Article
LA English
AB A novel procedure which allow the rapid screening of complex protein mixtures in cellular assays is described. A device has been developed which allows a convenient, simultaneous electroelution of separated proteins from whole SDS polyacrylamide gels into narrow chambers each containing single or a few protein bands. We have optimized the conditions of the procedure and have obtained an efficient removal of SDS, leading to non-toxic protein fractions in a physiological buffer suited for direct testing in cell cultures. The responses generated by stimulating lymphocytes with the purified products have been compared to the native protein and a corresponding preparation of protein transferred to nitrocellulose particles. The method was used to investigate murine T cell responses to secreted mycobacterial antigens during infection with M. ***tuberculosis*** . A immunodominant secreted protein fraction was purified in a semipreparative scale by the procedure and used to immunize mice. The specificity of and lymphokine production by T cells generated in these animals were investigated. The device developed has various applications and provides a tool for the possible identification of new T cell antigens of importance for protective immunity.

L6 ANSWER 60 OF 61 CAPLUS COPYRIGHT 2001 ACS
AN 1991:554780 CAPLUS
DN 115:154780
TI Proteins released from Mycobacterium ***tuberculosis*** during growth
AU ***Andersen, Peter*** ; Askgaard, Dorthe; Ljungqvist, Lene; Bennedsen, Joergen; Heron, Iver

CS Vaccine Dep., State Serum Inst., Copenhagen, DK-2300, Den.
SO Infect. Immun. (1991), 59(6), 1905-10
CODEN: INFIBR; ISSN: 0019-9567
DT Journal
LA English
AB Proteins secreted from M. ***tuberculosis*** during growth are believed to be important for protective immunity against ***tuberculosis*** . The growth of M. ***tuberculosis*** in an enriched liq. medium was investigated. The release of isocitrate dehydrogenase from the bacilli served as a marker of autolysis and was obsd. during the late logarithmic growth phase. The release of proteins during the culture period was investigated by ELISA and SDS-PAGE. Three major groups of proteins, which differed markedly with respect to profile of release and location in intact bacilli, were defined. A short-term filtrate devoid of autolytic products was defined and found to be composed of 33 major components. Five proteins were identified by monoclonal antibodies. Pronounced superoxide dismutase activity was detected in the filtrate. The enzyme was purified and identified as a dominating component of short-term filtrate.

L6 ANSWER 61 OF 61 CAPLUS COPYRIGHT 2001 ACS
AN 1991:227167 CAPLUS
DN 114:227167
TI T-cell proliferative response to antigens secreted by Mycobacterium ***tuberculosis***
AU ***Andersen, Peter*** ; Askgaard, Dorthe; Ljungovist, Lene; Bentzon, Michael Weis; Heron, Iver
CS Vaccine, Dep., Statens Seruminst., Copenhagen, DK-2300, Den.
SO Infect. Immun. (1991), 59(4), 1558-63
CODEN: INFIBR; ISSN: 0019-9567
DT Journal
LA English
AB An infection model of human ***tuberculosis*** was established with C57BL/6J mice. The lymphocyte proliferative responses to antigens from M. ***tuberculosis*** were investigated during the course of infection and compared with results obtained with a group of mice immunized with large amts. of killed bacteria. The two groups responded similarly to a no. of mycobacterial antigens, but marked differences in responses against secreted antigens were found; only infected mice responded vigorously to these. The responding lymphocyte subpopulation was made up of L3T4+ T lymphocytes under restriction of the Ia mol.

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E3 96 --> RASMUSSEN PETER/AU
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E5 1 RASMUSSEN PETER B/AU
E6 17 RASMUSSEN PETER BIRK/AU
E7 2 RASMUSSEN PETER CHRISTIAN/AU
E8 3 RASMUSSEN PETER D/AU
E9 2 RASMUSSEN PETER F/AU
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E11 1 RASMUSSEN PETER J/AU

E12 2 RASMUSSEN PETER MAX/AU

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L8 ANSWER 1 OF 7 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 1
AN 2001:302988 BIOSIS
DN PREV200100302988
TI Protection of mice with a ***tuberculosis*** subunit vaccine based on a fusion protein of antigen 85B and ESAT-6.
AU Olsen, Anja Weinreich; van Pinxteren, Laurens A. H.; Okkels, Limei Meng; ***Rasmussen, Peter Birk*** ; Andersen, Peter (1)
CS (1) Department of TB Immunology, Statens Serum Institut, Artillerivej 5, DK-2300, Copenhagen S: pa@ssi.dk Denmark
SO Infection and Immunity, (May, 2001) Vol. 69, No. 5, pp. 2773-2778. print. ISSN: 0019-9567.
DT Article
LA English
SL English
AB In this study, we investigated the potential of a ***tuberculosis*** subunit vaccine based on fusion proteins of the immunodominant antigens ESAT-6 and antigen 85B. When the fusion proteins were administered to mice in the adjuvant combination dimethyl dioctadecylammonium bromide-monophosphoryl lipid A, a strong dose-dependent immune response was induced to both single components as well as to the fusion proteins. The immune response induced was accompanied by high levels of protective immunity and reached the level of Mycobacterium bovis BCG-induced protection over a broad dose range. The vaccine induced efficient immunological memory, which remained stable 30 weeks postvaccination.

L8 ANSWER 2 OF 7 CAPLUS COPYRIGHT 2001 ACS
AN 1999:77692 CAPLUS
DN 130:165432
TI The antigenic protein LHP of Mycobacterium ***tuberculosis*** and the lhp gene encoding it and their diagnostic and prophylactic uses
IN Gicquel, Brigitte; Berthet, Francois-Xavier; Andersen, Peter; ***Rasmussen, Peter Birk***
PA Institut Pasteur, Fr.; Statens Serum Institut
SO PCT Int. Appl., 88 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO. KIND DATE APPLICATION NO. DATE

PI WO 9904005 A1 19990128 WO 1998-IB1091 19980716
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
AU 9881238 A1 19990210 AU 1998-81238 19980716
EP 1003870 A1 20000531 EP 1998-930967 19980716
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI
PRAI US 1997-52631 P 19970716
WO 1998-IB1091 W 19980716

AB The Mycobacterium ***tuberculosis*** gene encoding the antigenic protein LHP that is homologous to the L45 antigen of M. bovis, is cloned and characterized. The gene can be expressed from its own promoter in slow-growing (M. ***tuberculosis*** group) and fast-growing (M. smegmatis) mycobacteria. The LHP gene product, and antigenic peptides derived from it, can be manufd. for use in vaccines and to raise reagent antibodies for diagnostic use. The promoter of the lhp gene may be of use in the expression of foreign genes in Mycobacteria. Oligonucleotides derived from the promoter region may be useful as probes or primers in the detection of M. ***tuberculosis*** in a biol. sample. Anal. of the promoters driving expression of the closely linked lhp and orf1C genes of M. ***tuberculosis*** established that they form an operon. Use of the promoter to drive expression of a reporter gene in M. smegmatis is demonstrated. The protein is abundant in short-term (7 day) culture filtrates of M. ***tuberculosis*** .

RE.CNT 9
RE
(1) Ajinomoto Kk; EP 0400973 A 1990 CAPLUS
(3) Corixa Corp; WO 9709428 A 1997 CAPLUS
(4) Corixa Corp; WO 9709429 A 1997 CAPLUS
(5) Corixa Corp; WO 9816645 A 1998 CAPLUS
(6) Corixa Corp; WO 9816646 A 1998 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 3 OF 7 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 2
AN 2000:34114 BIOSIS
DN PREV200000034114
TI Differential T-cell recognition of native and recombinant Mycobacterium ***tuberculosis*** GroES.
AU Rosenkrands, Ida; Weldingh, Karin; Ravn, Pernille; Brandt, Lise; Hojrup, Peter; ***Rasmussen, Peter Birk*** ; Coates, Anthony R.; Singh, Mahavir; Mascagni, Paolo; Andersen, Peter (1)
CS (1) Department of TB Immunology, Statens Serum Institut, 5 Artillerivej, DK-2300, Copenhagen S Denmark
SO Infection and Immunity, (Nov., 1999) Vol. 67, No. 11, pp. 5552-5558. ISSN: 0019-9567.
DT Article
LA English

SL English

AB Mycobacterium ***tuberculosis*** GroES was purified from culture filtrate, and its identity was confirmed by immunoblot analysis and N-terminal sequencing. Comparing the immunological recognition of native and recombinant GroES, we found that whereas native GroES elicited a strong proliferative response and release of gamma interferon-gamma by peripheral blood mononuclear cells from healthy tuberculin reactors, the recombinant protein failed to do so. The same difference in immunological recognition was observed in a mouse model of TB infection. Both the native and recombinant preparations were recognized by mice immunized with the recombinant protein. Biochemical characterization including sodium dodecyl sulfate-polyacrylamide gel electrophoresis, two-dimensional electrophoresis, and mass spectrometry analysis of both proteins demonstrated no differences between the native and recombinant forms of GroES except for the eight additional N-terminal amino acids derived from the fusion partner inrecombinant GroES. The recombinant fusion protein, still tagged with the maltose binding protein, was recognized by T cells isolated from TB-infected mice if mixed with culture filtrate before affinity purification on an amylose column. The maltose binding protein treated in the same manner as a control preparation was not recognized. Based on the data presented, we suggest that the association of biologically active molecules from culture filtrate with the chaperone GroES may be responsible for the observed T-cell recognition of the native preparation.

L8 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2001 ACS

AN 1998:684968 CAPLUS

DN 129:300060

TI Novel antigens of Mycobacterium ***tuberculosis*** culture filtrates and the genes encoding and their diagnostic and prophylactic use

IN Andersen, Peter; Nielsen, Rikke; Rosenkrands, Ida; Weldingh, Karin; ***Rasmussen, Peter Birk*** ; Oettinger, Thomas; Florio, Walter

PA Statens Serum Institut, Den.

SO PCT Int. Appl., 264 pp.
CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9844119	A1	19981008	WO 1998-DK132	19980401
W: AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, CZ, DE, DE, DK, DK, EE, EE, ES, FI, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9868204	A1	19981022	AU 1998-68204	19980401
EP 972045	A1	20000119	EP 1998-913536	19980401
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
WO 9924577	A1	19990520	WO 1998-DK438	19981008

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

EP 1029053 A1 20000823 EP 1998-947412 19981008
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI

PRAI DK 1997-376 A 19970402
US 1997-44624 P 19970418
DK 1997-1277 A 19971110
US 1998-70488 P 19980105
WO 1998-DK132 W 19980401
WO 1998-DK438 W 19981008

AB Culture filtrate antigens of Mycobacterium ***tuberculosis*** are characterized and cDNAs encoding them are cloned. Some of the proteins are antigenic and suitable for use in vaccines and in diagnosis of infections, e.g. skin tests. A fusion protein of two of these antigens is a superior immunogen compared to the unfused proteins. Individual antigens from culture filtrates were identified by T cell mapping using T cells from memory immune mice. Genes for individual antigens were then cloned by screening a .lambda.gt11 expression vector with monoclonal antibodies. Manuf. of individual antigens with hexahistidine affinity labels is described.

L8 ANSWER 5 OF 7 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 3
AN 1998:393332 BIOSIS
DN PREV199800393332
TI Two-dimensional electrophoresis for analysis of Mycobacterium ***tuberculosis*** culture filtrate and purification and characterization of six novel proteins.
AU Weldingh, Karin; Rosenkrands, Ida; Jacobsen, Susanne; ***Rasmussen,*** *** Peter Birk*** ; Elhay, Martin J.; Andersen, Peter (1)
CS (1) Dep. TB Immunol., Statens Serum Inst., Artillerivej 5, DK-2300 Copenhagen Denmark
SO Infection and Immunity, (Aug., 1998) Vol. 66, No. 8, pp. 3492-3500. ISSN: 0019-9567.
DT Article
LA English
AB Culture filtrate from Mycobacterium ***tuberculosis*** contains molecules which promote high levels of protective immunity in animal models of subunit vaccination against ***tuberculosis*** . We have used two-dimensional electrophoresis for analysis and purification of six novel M. ***tuberculosis*** culture filtrate proteins (CFPs): CFP17, CFP20, CFP21, CFP22, CFP25, and CFP28. The proteins were tested for recognition by M. ***tuberculosis*** -reactive memory cells from different strains of inbred mice and for their capacity to induce a skin test response in M. ***tuberculosis*** -infected guinea pigs. CFP17, CFP20, CFP21 and CFP25 induced both a high gamma interferon release and a strong delayed-type hypersensitivity response, and CFP21 was broadly recognized by different strains of inbred mice. N-terminal sequences were obtained for the six proteins, and the corresponding genes were identified in the Sanger M.

tuberculosis genome database. In parallel we established a two-dimensional electrophoresis reference may of short-term culture filtrate components and mapped novel proteins as well as already-known CFP.

L8 ANSWER 6 OF 7 CAPLUS COPYRIGHT 2001 ACS
AN 1998:753589 CAPLUS
DN 130:120272
TI A Mycobacterium ***tuberculosis*** operon encoding ESAT-6 and a novel low-molecular-mass culture filtrate protein (CFP-10)
AU Berthet, Francois-Xavier; ***Rasmussen, Peter Birk*** ; Rosenkrands, Ida; Andersen, Peter; Gicquel, Brigitte
CS Unite de Genetique Mycobacterienne, Institut Pasteur, Paris, 75724, Fr.
SO Microbiology (Reading, U. K.) (1998), 144(11), 3195-3203
CODEN: MROBEO; ISSN: 1350-0872
PB Society for General Microbiology
DT Journal
LA English
AB The early secreted antigenic target 6 kDa protein (ESAT-6) is a potent T-cell protein antigen synthesized by Mycobacterium ***tuberculosis*** . Its corresponding gene (esat-6) is located in RD1, a 10kb DNA region deleted in the attenuated ***tuberculosis*** vaccine strain Mycobacterium bovis BCG. The promoter region of M. ***tuberculosis*** esat-6 was cloned and characterized. A new gene, designated lhp and cotranscribed with esat-6, was identified. Moreover, computer searches in the M. ***tuberculosis*** genome identified 13 genes related to the lhp/esat-6 operon, defining a novel gene family. The transcription initiation sites of the lhp/esat-6 operon were mapped using M. ***tuberculosis*** RNA. The corresponding promoter signals were not recognized in Mycobacterium smegmatis, in which transcription of lhp/esat-6 is initiated at different locations. The M. ***tuberculosis*** lhp gene product was identified as CFP-10, a low-mol.-mass protein found in the short-term culture filtrate. These results show that the genes encoding CFP-10 and ESAT-6 are transcribed together in M. ***tuberculosis*** and that both code for small exported proteins.
RE.CNT 22
RE
(1) Andersen, P; Infect Immun 1991, V59, P1558 CAPLUS
(2) Andersen, P; J Immunol 1995, V154, P3359 CAPLUS
(3) Bashyam, M; Biotechniques 1994, V17, P834 CAPLUS
(4) Bashyam, M; J Bacteriol 1996, V178, P4847 CAPLUS
(5) Berthet, F; Microbiology 1995, V141, P2123 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 7 OF 7 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 4
AN 1998:304925 BIOSIS
DN PREV199800304925
TI Identification and characterization of a 29-kilodalton protein from Mycobacterium ***tuberculosis*** culture filtrate recognized by mouse memory effector cells.
AU Rosenkrands, Ida; ***Rasmussen, Peter Birk*** ; Carnio, Markus; Jacobsen, Susanne; Theisen, Michael; Andersen, Peter (1)
CS (1) Dep. TB Immunol., Statens Serum Inst., 5 Artillerivej, DK-2300 Copenhagen S Denmark

SO Infection and Immunity, (June, 1998) Vol. 66, No. 6, pp. 2728-2735.
ISSN: 0019-9567.
DT Article
LA English
AB Culture filtrate proteins from Mycobacterium ***tuberculosis*** induce protective immunity in various animal models of ***tuberculosis*** . Two molecular mass regions (6 to 10 kDa and 24 to 36 kDa) of short-term culture filtrate are preferentially recognized by Th1 cells in animal models as well as by patients with minimal disease. In the present study, the 24- to 36-kDa region has been studied, and the T-cell reactivity has been mapped in detail. Monoclonal antibodies were generated, and one monoclonal antibody, HYB 71-2, with reactivity against a 29-kDa antigen located in the highly reactive region below the antigen 85 complex was selected. The 29-kDa antigen (CFP29) was purified from M. ***tuberculosis*** short-term culture filtrate by thiophilic adsorption chromatography, anion-exchange chromatography, and gel filtration. In its native form, CFP29 forms a polymer with a high molecular mass. CFP29 was mapped in two-dimensional electrophoresis gels as three distinct spots just below the antigen 85 complex component MPT59. CFP29 is present in both culture filtrate and the membrane fraction from M. ***tuberculosis*** , suggesting that this antigen is released from the envelope to culture filtrate during growth. Determination of the N-terminal amino acid sequence allowed cloning and sequencing of the cfp29 gene. The nucleotide sequence showed 62% identity to the bacteriocin Linocin from Brevibacterium linens. Purified recombinant histidine-tagged CFP29 and native CFP29 had similar T-cell stimulatory properties, and they both elicited the release of high levels of gamma interferon from mouse memory effector cells isolated during the recall of protective immunity to ***tuberculosis*** . Interspecies analysis by immunoblotting and PCR demonstrated that CFP29 is widely distributed in mycobacterial species.

=> s tuberculosis and (lhp or cfp10)
L9 37 TUBERCULOSIS AND (LHP OR CFP10)

=> dup rem l9
PROCESSING COMPLETED FOR L9
L10 11 DUP REM L9 (26 DUPLICATES REMOVED)

=> d bib ab kwic 1-
YOU HAVE REQUESTED DATA FROM 11 ANSWERS - CONTINUE? Y/(N):y

L10 ANSWER 1 OF 11 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 1
AN 2001:116597 BIOSIS
DN PREV200100116597
TI Enumeration of T cells specific for RD1-encoded antigens suggests a high prevalence of latent Mycobacterium ***tuberculosis*** infection in healthy urban Indians.
AU Lalvani, Ajit (1); Nagvenkar, Punam; Udwadia, Zarir; Pathan, Ansar A.; Wilkinson, Katalin A.; Shastri, Jayanthi S.; Ewer, Katie; Hill, Adrian V. S.; Mehta, Ajita; Rodrigues, Camilla
CS (1) Nuffield Dept. of Clinical Medicine, John Radcliffe Hospital, University of Oxford, Level 7, Oxford, OX3 9DU: ajit.lalvani@ndm.ox.ac.uk UK

SO Journal of Infectious Diseases, (1 February, 2001) Vol. 183, No. 3, pp. 469-477. print.
ISSN: 0022-1899.
DT Article
LA English
SL English
AB Knowledge of the prevalence of latent Mycobacterium ***tuberculosis*** infection is crucial for effective ***tuberculosis*** control, but tuberculin skin test surveys have major limitations, including poor specificity because of the broad antigenic cross-reactivity of tuberculin. The M. ***tuberculosis*** RD1 genomic segment encodes proteins, such as early secretory antigenic target (ESAT)-6, that are absent from M. bovis bacille Calmette-Guerin (BCG) and most environmental mycobacteria. We recently identified circulating ESAT-6-specific T cells as an accurate marker of M. ***tuberculosis*** infection. Here, interferon-gamma-secreting T cells specific for peptides derived from ESAT-6 and a second RD1 gene product, ***CFP10*** , were enumerated in 100 prospectively recruited healthy adults in Bombay (Mumbai), India. Eighty percent responded to gtoreq1 antigen, and many donors had high frequencies of T cells that were specific for certain immunodominant peptides. In contrast, of 40 mostly BCG-vaccinated, United Kingdom-resident healthy adults, none responded to either antigen. This study suggests an 80% prevalence of latent M. ***tuberculosis*** infection in urban India.
TI Enumeration of T cells specific for RD1-encoded antigens suggests a high prevalence of latent Mycobacterium ***tuberculosis*** infection in healthy urban Indians.
AB Knowledge of the prevalence of latent Mycobacterium ***tuberculosis*** infection is crucial for effective ***tuberculosis*** control, but tuberculin skin test surveys have major limitations, including poor specificity because of the broad antigenic cross-reactivity of tuberculin. The M. ***tuberculosis*** RD1 genomic segment encodes proteins, such as early secretory antigenic target (ESAT)-6, that are absent from M. bovis bacille Calmette-Guerin (BCG) and most environmental mycobacteria. We recently identified circulating ESAT-6-specific T cells as an accurate marker of M. ***tuberculosis*** infection. Here, interferon-gamma-secreting T cells specific for peptides derived from ESAT-6 and a second RD1 gene product, ***CFP10*** , were enumerated in 100 prospectively recruited healthy adults in Bombay (Mumbai), India. Eighty percent responded to gtoreq1 antigen, and many. . . mostly BCG-vaccinated, United Kingdom-resident healthy adults, none responded to either antigen. This study suggests an 80% prevalence of latent M. ***tuberculosis*** infection in urban India.
IT . . .
(Population Studies)
IT Parts, Structures, & Systems of Organisms
T cells: blood and lymphatics, enumeration, immune system
IT Diseases
Mycobacterium ***tuberculosis*** infection: bacterial disease
IT Chemicals & Biochemicals
CFP10 ; ESAT-6; RD1-encoded antigens; interferon-gamma
IT Alternate Indexing
Mycobacterium Infections (MeSH)
ORGN . . .
Vertebrata, Chordata, Animalia; Mycobacteriaceae: Mycobacteria, Actinomycetes and Related Organisms, Eubacteria, Bacteria,

Microorganisms
ORGN Organism Name
Mycobacterium bovis (Mycobacteriaceae): pathogen; Mycobacterium ***tuberculosis*** (Mycobacteriaceae): latent, pathogen; human (Hominidae): healthy, indian, urban
ORGN Organism Superterms
Animals; Bacteria; Chordates; Eubacteria; Humans; Mammals; Microorganisms; Primates; Vertebrates

L10 ANSWER 2 OF 11 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
AN 2001163910 EMBASE
TI Performance of whole blood IFN-.gamma. test for ***tuberculosis*** diagnosis based on PPD or the specific antigens ESAT-6 and CFP-10.
AU Brock I.; Munk M.E.; Kok-Jensen A.; Andersen P.
CS Dr. P. Andersen, Dept. of Tuberculosis Immunology, Statens Serum Institute, 5 Artillerivej, 2300 Copenhagen S, Denmark. PA@SSI.DK
SO International Journal of Tuberculosis and Lung Disease, (2001) 5/5 (462-467).
Refs: 21
ISSN: 1027-3719 CODEN: IJTDFO
CY France
DT Journal; Article
FS 015 Chest Diseases, Thoracic Surgery and Tuberculosis
026 Immunology, Serology and Transplantation
027 Biophysics, Bioengineering and Medical Instrumentation
LA English
SL English; French; Spanish
AB OBJECTIVE: To evaluate the QuantiFERON-TB.RTM. test in BCG-vaccinated, non-BCG-vaccinated and ***tuberculosis*** (TB) patient donor groups, and to compare its diagnostic performance with that of a blood test based on the Mycobacterium ***tuberculosis*** specific antigens ESAT-6 and CFP-10. DESIGN: Analysis of the IFN-.gamma. responses of whole blood cells from BCG-vaccinated or non-BCG-vaccinated donors or patients with ***tuberculosis*** , stimulated with PPD, ESAT-6 or CFP-10 antigens, and evaluation of the specificity and sensitivity of the test. RESULTS: None of the non-vaccinated donors showed positive responses to M. ***tuberculosis*** -PPD, ESAT-6 or CFP-10. In BCG-vaccinated donors, 9/19 (47%) donors responded to the QuantiFERON-TB.RTM. test based on M. ***tuberculosis*** -PPD, whereas 2/19 (10.5%) responded to either ESAT-6 or CFP-10. Comparable levels of sensitivity were obtained with the QuantiFERON-TB.RTM. test based on M. ***tuberculosis*** -PPD (79%) and ESAT-6 or CFP-10 antigens (72%). CONCLUSION: Our results demonstrate that the whole blood test based on M. ***tuberculosis*** -PPD did not efficiently distinguish BCG-vaccinated donors from individuals with disease due to M. ***tuberculosis*** . The introduction of new recombinant antigens specific for M. ***tuberculosis*** , such as ESAT-6 or CFP-10, should increase the specificity of the whole blood test and enable discrimination between TB infection, atypical mycobacterial reactivity and reactivity due to BCG vaccination. Such a test would provide a quantum improvement over the current practice of using the tuberculin skin test for TB control and elimination.
TI Performance of whole blood IFN-.gamma. test for ***tuberculosis*** diagnosis based on PPD or the specific antigens ESAT-6 and CFP-10.
AB OBJECTIVE: To evaluate the QuantiFERON-TB.RTM. test in BCG-vaccinated, non-BCG-vaccinated and ***tuberculosis*** (TB) patient donor groups,

and to compare its diagnostic performance with that of a blood test based on the Mycobacterium ***tuberculosis*** specific antigens ESAT-6 and CFP-10. DESIGN: Analysis of the IFN-.gamma. responses of whole blood cells from BCG-vaccinated or non-BCG-vaccinated donors or patients with ***tuberculosis*** , stimulated with PPD, ESAT-6 or CFP-10 antigens, and evaluation of the specificity and sensitivity of the test. RESULTS: None of the non-vaccinated donors showed positive responses to M. ***tuberculosis*** -PPD, ESAT-6 or CFP-10. In BCG-vaccinated donors, 9/19 (47%) donors responded to the QuantiFERON-TB.RTM. test based on M. ***tuberculosis*** -PPD, whereas 2/19 (10.5%) responded to either ESAT-6 or CFP-10. Comparable levels of sensitivity were obtained with the QuantiFERON-TB.RTM. test based on M. ***tuberculosis*** -PPD (79%) and ESAT-6 or CFP-10 antigens (72%). CONCLUSION: Our results demonstrate that the whole blood test based on M. ***tuberculosis*** -PPD did not efficiently distinguish BCG-vaccinated donors from individuals with disease due to M. ***tuberculosis*** . The introduction of new recombinant antigens specific for M. ***tuberculosis*** , such as ESAT-6 or CFP-10, should increase the specificity of the whole blood test and enable discrimination between TB infection,. . .

CT Medical Descriptors:
****tuberculosis: DI, diagnosis***
****tuberculosis: ET, etiology***
BCG vaccination
diagnostic value
diagnostic accuracy
Mycobacterium tuberculosis
immunostimulation
sensitivity and specificity
immunoreactivity
tuberculin test
human
controlled study
adult
article
priority journal
*gamma interferon
*tuberculin
*recombinant antigen
*ESAT antigen
****CFP10 antigen***
BCG vaccine
unclassified drug

L10 ANSWER 3 OF 11 CAPLUS COPYRIGHT 2001 ACS DUPLICATE 2
AN 2001:26331 CAPLUS
DN 134:206474
TI Classically restricted human CD8+ T lymphocytes derived from Mycobacterium ***tuberculosis*** -infected cells: definition of antigenic specificity
AU Lewinsohn, David M.; Zhu, Liqing; Madison, Valerie J.; Dillon, Davin C.; Fling, Steven P.; Reed, Steven G.; Grabstein, Kenneth H.; Alderson, Mark R.
CS Division of Pulmonary and Critical Care Medicine, Department of Molecular Microbiology and Immunology, Oregon Health Sciences University/Portland Veterans Affairs Medical Center, Portland, OR, 97207, USA
SO J. Immunol. (2001), 166(1), 439-446

CODEN: JOIMA3; ISSN: 0022-1767
PB American Association of Immunologists
DT Journal
LA English
AB Previous studies in murine and human models have suggested an important role for HLA Ia-restricted CD8+ T cells in host defense to Mycobacterium ***tuberculosis*** (Mtb). Therefore, understanding the Ags presented via HLA-Ia will be important in understanding the host response to Mtb and in rational vaccine design. We have used monocyte-derived dendritic cells in a limiting diln. anal. to generate Mtb-specific CD8+ T cells. Two HLA-Ia-restricted CD8+ T cell clones derived by this method were selected for detailed anal. One was HLA-B44 restricted, and the other was HLA-B14 restricted. Both were found to react with Mtb-infected, but not bacillus Calmette-Guerin-infected, targets. For both these clones, the Ag was identified as culture filtrate protein 10 (***CFP10***)/Mtb11, a 10.8-kDa protein not expressed by bacillus Calmette-Guerin. Both clones were inhibited by the anti-class I Ab and anti-HLA-B,C Abs. Using a panel of ***CFP10*** /Mtb11-derived 15-aa peptides overlapping by 11 aa, the region contg. the epitopes for both clones has been defined. Minimal 10-aa epitopes were defined for both clones. CD8+ effector cells specific for these two epitopes are present at high frequency in the circulating pool. Moreover, the CD8+ T cell response to ***CFP10*** /Mtb11 can be largely accounted for by the two epitopes defined herein, suggesting that this is the immunodominant response for this purified protein deriv.-pos. donor. This study represents the first time CD8+ T cells generated against Mtb-infected APC have been used to elucidate an Mtb-specific CD8+ T cell Ag.
RE.CNT 37
RE
(1) Alderson, M; J Exp Med 2000, V191, P551 CAPLUS
(3) Behar, S; J Exp Med 1999, V189, P1973 CAPLUS
(4) Berthet, F; Microbiology 1998, V144, P3195 CAPLUS
(5) Coler, R; J Immunol 1998, V161, P2356 CAPLUS
(6) Dillon, D; Infect Immun 1999, V67, P2941 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT
TI Classically restricted human CD8+ T lymphocytes derived from Mycobacterium ***tuberculosis*** -infected cells: definition of antigenic specificity
AB Previous studies in murine and human models have suggested an important role for HLA Ia-restricted CD8+ T cells in host defense to Mycobacterium ***tuberculosis*** (Mtb). Therefore, understanding the Ags presented via HLA-Ia will be important in understanding the host response to Mtb and in rational vaccine design. We have used monocyte-derived dendritic cells in a limiting diln. anal. to generate Mtb-specific CD8+ T cells. Two HLA-Ia-restricted CD8+ T cell clones derived by this method were selected for detailed anal. One was HLA-B44 restricted, and the other was HLA-B14 restricted. Both were found to react with Mtb-infected, but not bacillus Calmette-Guerin-infected, targets. For both these clones, the Ag was identified as culture filtrate protein 10 (***CFP10***)/Mtb11, a 10.8-kDa protein not expressed by bacillus Calmette-Guerin. Both clones were inhibited by the anti-class I Ab and anti-HLA-B,C Abs. Using a panel of ***CFP10*** /Mtb11-derived 15-aa peptides overlapping by 11 aa, the region contg. the epitopes for both clones has been defined. Minimal 10-aa epitopes were defined for both clones. CD8+ effector cells specific for these two epitopes are present at high frequency in the circulating pool. Moreover, the CD8+ T cell response to ***CFP10*** /Mtb11 can be

largely accounted for by the two epitopes defined herein, suggesting that this is the immunodominant response for this purified protein deriv.-pos. donor. This study represents the first time CD8+ T cells generated against Mtb-infected APC have been used to elucidate an Mtb-specific CD8+ T cell Ag.

IT CD8-positive T cell
MHC restriction
Mycobacterium ***tuberculosis***
(classically restricted human CD8+ T lymphocytes derived from Mycobacterium ***tuberculosis*** -infected cells: definition of antigenic specificity)

IT Vaccines
(classically restricted human CD8+ T lymphocytes derived from Mycobacterium ***tuberculosis*** -infected cells: definition of antigenic specificity in relation to)

IT Proteins, specific or class
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(culture filtrate protein ***CFP10*** ; classically restricted human CD8+ T lymphocytes derived from Mycobacterium ***tuberculosis*** -infected cells: definition of antigenic specificity)

IT T cell (lymphocyte)
(infection; classically restricted human CD8+ T lymphocytes derived from Mycobacterium ***tuberculosis*** -infected cells: definition of antigenic specificity)

IT Epitopes
(mapping; classically restricted human CD8+ T lymphocytes derived from Mycobacterium ***tuberculosis*** -infected cells: definition of antigenic specificity)

IT 328238-12-6 328238-13-7
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(classically restricted human CD8+ T lymphocytes derived from Mycobacterium ***tuberculosis*** -infected cells: definition of antigenic specificity)

L10 ANSWER 4 OF 11 CAPLUS COPYRIGHT 2001 ACS DUPLICATE 3
AN 2001:381343 CAPLUS
TI Biotechnology in the development of new vaccines and diagnostic reagents against ***tuberculosis***
AU Mustafa, A. S.
CS Department of Microbiology, Faculty of Medicine, Kuwait University, Safat, 13110, Kuwait
SO Curr. Pharm. Biotechnol. (2001), 2(2), 157-173
CODEN: CPBUBP; ISSN: 1389-2010
PB Bentham Science Publishers Ltd.
DT Journal
LA English
AB ***Tuberculosis*** (TB) is a disease of global concern. About one third of the world population is infected with Mycobacterium ***tuberculosis*** . Every year, approx. 8 million people get the disease and 2 million die of TB. The currently available vaccine against TB is the attenuated strain of Mycobacterium bovis, Bacillus Calmette Guerin (BCG), which has failed to provide consistent protection in different parts of the world. The commonly used diagnostic reagent for TB is the purified protein deriv. (PPD) of M. ***tuberculosis*** , which is nonspecific because of the presence of antigens crossreactive with BCG

and environmental mycobacteria. Thus there is a need to identify M. ***tuberculosis*** antigens as candidates for new protective vaccines and specific diagnostic reagents against TB. By using the techniques of recombinant DNA, synthetic peptides, antigen-specific antibodies and T cells etc., several major antigens of M. ***tuberculosis*** have been identified, e.g. heat shock protein (hsp)60, hsp70, Ag85, ESAT-6 and ***CFP10*** etc. These antigens have shown promise as new candidate vaccines and/or diagnostic reagents against TB. In addn., recent comparisons of the genome sequence of M. ***tuberculosis*** with BCG and other mycobacteria have unraveled M. ***tuberculosis*** specific regions and genes. Expression and immunol. evaluation of these regions and genes can potentially identify most of the antigens of M. ***tuberculosis*** important for developing new vaccines and specific diagnostic reagents against TB. Moreover, advances in identification of proper adjuvant and delivery systems can potentially overcome the problem of poor immunogenicity/short-lived immunity assocd. with protein and peptide based vaccines. In conclusion, the advances in biotechnol. are contributing significantly in the process of developing new protective vaccines and diagnostic reagents against TB.

RE.CNT 120

RE

(1) Ahmad, S; Scand J Immunol 1999, V50(5), P510 CAPLUS
(2) Ahmad, S; Scand J Immunol 1999, V49(5), P515 CAPLUS
(3) Andersen, P; Infect Immun 1994, V62(6), P2536 CAPLUS
(4) Andersen, P; J Immunol 1995, V154(7), P3359 CAPLUS
(5) Andersen, P; Scand J Immunol 1997, V45(2), P115 CAPLUS

ALL CITATIONS AVAILABLE IN THE RE FORMAT

TI Biotechnology in the development of new vaccines and diagnostic reagents against ***tuberculosis***

AB ***Tuberculosis*** (TB) is a disease of global concern. About one third of the world population is infected with Mycobacterium ***tuberculosis*** . Every year, approx. 8 million people get the disease and 2 million die of TB. The currently available vaccine against TB is the attenuated strain of Mycobacterium bovis, Bacillus Calmette Guerin (BCG), which has failed to provide consistent protection in different parts of the world. The commonly used diagnostic reagent for TB is the purified protein deriv. (PPD) of M. ***tuberculosis*** , which is nonspecific because of the presence of antigens crossreactive with BCG and environmental mycobacteria. Thus there is a need to identify M. ***tuberculosis*** antigens as candidates for new protective vaccines and specific diagnostic reagents against TB. By using the techniques of recombinant DNA, synthetic peptides, antigen-specific antibodies and T cells etc., several major antigens of M. ***tuberculosis*** have been identified, e.g. heat shock protein (hsp)60, hsp70, Ag85, ESAT-6 and ***CFP10*** etc. These antigens have shown promise as new candidate vaccines and/or diagnostic reagents against TB. In addn., recent comparisons of the genome sequence of M. ***tuberculosis*** with BCG and other mycobacteria have unraveled M. ***tuberculosis*** specific regions and genes. Expression and immunol. evaluation of these regions and genes can potentially identify most of the antigens of M. ***tuberculosis*** important for developing new vaccines and specific diagnostic reagents against TB. Moreover, advances in identification of proper adjuvant and delivery systems can potentially overcome the problem of poor immunogenicity/short-lived immunity assocd. with protein and peptide based vaccines. In conclusion, the advances in biotechnol. are

contributing significantly in the process of developing new protective vaccines and diagnostic reagents against TB.

L10 ANSWER 5 OF 11 CAPLUS COPYRIGHT 2001 ACS
AN 2000:358998 CAPLUS
DN 133:118838
TI Antigenic equivalence of human T-cell responses to Mycobacterium ***tuberculosis*** -specific RD1-encoded protein antigens ESAT-6 and culture filtrate protein 10 and to mixtures of synthetic peptides
AU Arend, Sandra M.; Geluk, Annemieke; Van Meijgaarden, Krista E.; Van Dissel, Jaap T.; Theisen, Michael; Andersen, Peter; Ottenhoff, Tom H. M.
CS Department of Infectious Diseases, Leiden University Medical Center, Leiden, 2300, Neth.
SO Infect. Immun. (2000), 68(6), 3314-3321
CODEN: INFIBR; ISSN: 0019-9567
PB American Society for Microbiology
DT Journal
LA English
AB The early secreted antigenic target 6-kDa protein (ESAT-6) and culture filtrate protein 10 (CFP-10) are promising antigens for reliable immunodiagnosis of ***tuberculosis*** . Both antigens are encoded by RD1, a genomic region present in all strains of Mycobacterium ***tuberculosis*** and M. bovis but lacking in all M. bovis bacillus Calmette-Guerin vaccine strains. Prodn. and purifn. of recombinant antigens are laborious and costly, precluding rapid and large-scale testing. Aiming to develop alternative diagnostic reagents, we have investigated whether recombinant ESAT-6 (rESAT-6) and recombinant CFP-10 (rCFP-10) can be replaced with corresponding mixts. of overlapping peptides spanning the complete amino acid sequence of each antigen. Proliferation of M. ***tuberculosis*** -specific human T-cell lines in response to rESAT-6 and rCFP-10 and that in response to the corresponding peptide mixts. were almost completely correlated ($r = 0.96$, $P < 0.0001$ for ESAT-6; $r = 0.98$, $P < 0.0001$ for CFP-10). More importantly, the same was found when gamma interferon prodn. by peripheral blood mononuclear cells in response to these stimuli was analyzed ($r = 0.89$, $P < 0.0001$ for ESAT-6; $r = 0.89$, $P < 0.0001$ for CFP-10). Whole protein antigens and the peptide mixts. resulted in identical sensitivity and specificity for detection of infection with M. ***tuberculosis*** . The peptides in each mixt. contributing to the overall response varied between individuals with different HLA-DR types. Interestingly, responses to CFP-10 were significantly higher in the presence of HLA-DR15, which is the major subtype of DR2. These results show that mixts. of synthetic overlapping peptides have potency equiv. to that of whole ESAT-6 and CFP-10 for sensitive and specific detection of infection with M. ***tuberculosis*** , and peptides have the advantage of faster prodn. at lower cost.
RE.CNT 30
RE
(1) Andersen, P; Infect Immun 1991, V59, P1905 CAPLUS
(6) Behr, M; Science 1999, V284, P1520 CAPLUS
(7) Berthet, F; Microbiology 1998, V144, P3195 CAPLUS
(9) Brosch, R; Infect Immun 1998, V66, P2221 CAPLUS
(10) Cole, S; Nature 1998, V393, P537 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT
TI Antigenic equivalence of human T-cell responses to Mycobacterium ***tuberculosis*** -specific RD1-encoded protein antigens ESAT-6 and

culture filtrate protein 10 and to mixtures of synthetic peptides

AB The early secreted antigenic target 6-kDa protein (ESAT-6) and culture filtrate protein 10 (CFP-10) are promising antigens for reliable immunodiagnosis of ***tuberculosis*** . Both antigens are encoded by RD1, a genomic region present in all strains of Mycobacterium ***tuberculosis*** and M. bovis but lacking in all M. bovis bacillus Calmette-Guerin vaccine strains. Prodn. and purifn. of recombinant antigens are laborious and costly, precluding rapid and large-scale testing. Aiming to develop alternative diagnostic reagents, we have investigated whether recombinant ESAT-6 (rESAT-6) and recombinant CFP-10 (rCFP-10) can be replaced with corresponding mixts. of overlapping peptides spanning the complete amino acid sequence of each antigen. Proliferation of M. ***tuberculosis*** -specific human T-cell lines in response to rESAT-6 and rCFP-10 and that in response to the corresponding peptide mixts. were almost completely correlated ($r = 0.96$, $P < 0.0001$ for ESAT-6; $r = 0.98$, $P < 0.0001$ for CFP-10). More importantly, the same was found when gamma interferon prodn. by peripheral blood mononuclear cells in response to these stimuli was analyzed ($r = 0.89$, $P < 0.0001$ for ESAT-6; $r = 0.89$, $P < 0.0001$ for CFP-10). Whole protein antigens and the peptide mixts. resulted in identical sensitivity and specificity for detection of infection with M. ***tuberculosis*** . The peptides in each mixt. contributing to the overall response varied between individuals with different HLA-DR types. Interestingly, responses to CFP-10 were significantly higher in the presence of HLA-DR15, which is the major subtype of DR2. These results show that mixts. of synthetic overlapping peptides have potency equiv. to that of whole ESAT-6 and CFP-10 for sensitive and specific detection of infection with M. ***tuberculosis*** , and peptides have the advantage of faster prodn. at lower cost.

ST Mycobacterium ESAT6 ***CFP10*** antigen peptide T cell infection diagnosis

IT Proteins, specific or class
RL: BPR (Biological process); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(CFP-10 (culture filtrate protein 10); antigenic equivalence of human T-cell responses to Mycobacterium ***tuberculosis*** -specific RD1-encoded antigens ESAT-6 and culture filtrate protein 10 and to mixts. of synthetic peptides)

IT Antigens
RL: BPR (Biological process); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(ESAT-6; antigenic equivalence of human T-cell responses to Mycobacterium ***tuberculosis*** -specific RD1-encoded antigens ESAT-6 and culture filtrate protein 10 and to mixts. of synthetic peptides)

IT Histocompatibility antigens
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(HLA-DR2, -DR15 allele; antigenic equivalence of human T-cell responses to Mycobacterium ***tuberculosis*** -specific RD1-encoded antigens ESAT-6 and culture filtrate protein 10 and to mixts. of synthetic peptides depending on)

IT Histocompatibility antigens
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(HLA-DR; antigenic equivalence of human T-cell responses to Mycobacterium ***tuberculosis*** -specific RD1-encoded antigens ESAT-6 and culture filtrate protein 10 and to mixts. of synthetic

peptides depending on)
IT Mycobacterium ***tuberculosis***
T cell (lymphocyte)
(antigenic equivalence of human T-cell responses to Mycobacterium ***tuberculosis*** -specific RD1-encoded antigens ESAT-6 and culture filtrate protein 10 and to mixts. of synthetic peptides)
IT Peptides, biological studies
RL: BPN (Biosynthetic preparation); BPR (Biological process); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(antigenic equivalence of human T-cell responses to Mycobacterium ***tuberculosis*** -specific RD1-encoded antigens ESAT-6 and culture filtrate protein 10 and to mixts. of synthetic peptides)
IT Diagnosis
(antigenic equivalence of human T-cell responses to Mycobacterium ***tuberculosis*** -specific RD1-encoded antigens ESAT-6 and culture filtrate protein 10 and to mixts. of synthetic peptides for)
IT ***Tuberculosis***
(antigenic equivalence of human T-cell responses to Mycobacterium ***tuberculosis*** -specific RD1-encoded antigens ESAT-6 and culture filtrate protein 10 and to mixts. of synthetic peptides for diagnosis of)
IT T cell (lymphocyte)
(proliferation; antigenic equivalence of human T-cell responses to Mycobacterium ***tuberculosis*** -specific RD1-encoded antigens ESAT-6 and culture filtrate protein 10 and to mixts. of synthetic peptides)
IT Interferons
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(.gamma.; antigenic equivalence of human T-cell responses to Mycobacterium ***tuberculosis*** -specific RD1-encoded antigens ESAT-6 and culture filtrate protein 10 and to mixts. of synthetic peptides and formation of)
IT 285120-39-0P 285120-40-3P 285120-41-4P 285120-42-5P 285120-43-6P 285120-44-7P 285120-45-8P 285120-46-9P 285120-47-0P
RL: BPN (Biosynthetic preparation); BPR (Biological process); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(CFP-10; antigenic equivalence of human T-cell responses to Mycobacterium ***tuberculosis*** -specific RD1-encoded antigens ESAT-6 and culture filtrate protein 10 and to mixts. of synthetic peptides)
IT 183273-40-7P 219842-19-0P 219842-20-3P 285120-33-4P 285120-34-5P 285120-35-6P 285120-36-7P 285120-37-8P 285120-38-9P
RL: BPN (Biosynthetic preparation); BPR (Biological process); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(ESAT-6; antigenic equivalence of human T-cell responses to Mycobacterium ***tuberculosis*** -specific RD1-encoded antigens ESAT-6 and culture filtrate protein 10 and to mixts. of synthetic peptides)

L10 ANSWER 6 OF 11 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 4

AN 2000:455712 BIOSIS
DN PREV200000455712
TI Molecular and immunological characterization of Mycobacterium ***tuberculosis*** CFP-10, an immunodiagnostic antigen missing in Mycobacterium bovis BCG.
AU Dillon, Davin C. (1); Alderson, Mark R.; Day, Craig H.; Bement, Teresa; Campos-Neto, Antonio; Skeiky, Yasir A. W.; Vedvick, Thomas; Badaro, Roberto; Reed, Steven G.; Houghton, Raymond
CS (1) Corixa Corp., 1124 Columbia St., Seattle, WA, 98104 USA
SO Journal of Clinical Microbiology, (September, 2000) Vol. 38, No. 9, pp. 3285-3290. print.
ISSN: 0095-1137.
DT Article
LA English
SL English
AB In order to identify antigens that may be used in the serodiagnosis of active ***tuberculosis*** (TB), we screened a Mycobacterium ***tuberculosis*** genomic expression library with a pool of sera from patients diagnosed with active pulmonary TB. The sera used lacked reactivity with a recombinant form of the M. ***tuberculosis*** 38-kDa antigen (r38kDa), and the goal was to identify antigens that might complement r38kDa in a serodiagnostic assay. Utilizing this strategy, we identified a gene, previously designated ***lhp*** , which encodes a 100-amino-acid protein referred to as culture filtrate protein 10 (CFP-10). The ***lhp*** gene is located directly upstream of esat-6, within a region missing in M. bovis BCG. Immunoblot analysis demonstrated that CFP-10 is present in M. ***tuberculosis*** CFP, indicating that it is likely a secreted or shed antigen. Purified recombinant CFP-10 (rCFP-10) was shown to be capable of detecting specific antibody in a percentage of TB patients that lack reactivity with r38kDa, most notably in smear-negative cases, where sensitivity was increased from 21% for r38kDa alone to 40% with the inclusion of rCFP-10. In smear-positive patient sera, sensitivity was increased from 49% for r38kDa alone to 58% with the inclusion of rCFP-10. In addition, rCFP-10 was shown to be a potent T-cell antigen, eliciting proliferative responses and gamma interferon production from peripheral blood mononuclear cells in 70% of purified protein derivative-positive individuals without evident disease. The responses to this antigen argue for the inclusion of rCFP-10 in a polyvalent serodiagnostic test for detection of active TB infection. rCFP-10 could also contribute to the development of a recombinant T-cell diagnostic test capable of detecting exposure to M. ***tuberculosis***
.

TI Molecular and immunological characterization of Mycobacterium ***tuberculosis*** CFP-10, an immunodiagnostic antigen missing in Mycobacterium bovis BCG.
AB In order to identify antigens that may be used in the serodiagnosis of active ***tuberculosis*** (TB), we screened a Mycobacterium ***tuberculosis*** genomic expression library with a pool of sera from patients diagnosed with active pulmonary TB. The sera used lacked reactivity with a recombinant form of the M. ***tuberculosis*** 38-kDa antigen (r38kDa), and the goal was to identify antigens that might complement r38kDa in a serodiagnostic assay. Utilizing this strategy, we identified a gene, previously designated ***lhp*** , which encodes a 100-amino-acid protein referred to as culture filtrate protein 10 (CFP-10). The ***lhp*** gene is located directly upstream of esat-6,

within a region missing in M. bovis BCG. Immunoblot analysis demonstrated that CFP-10 is present in M. ***tuberculosis*** CFP, indicating that it is likely a secreted or shed antigen. Purified recombinant CFP-10 (rCFP-10) was shown to be capable. . . infection. rCFP-10 could also contribute to the development of a recombinant T-cell diagnostic test capable of detecting exposure to M. ***tuberculosis*** .

IT Major Concepts
Biochemistry and Molecular Biophysics; Infection; Clinical Immunology (Human Medicine, Medical Sciences)

IT Diseases
tuberculosis : bacterial disease

IT Chemicals & Biochemicals
BCG: Mycobacterium bovis; CFP-10 [culture filtrate protein 10]: T-cell antigen, immunodiagnostic antigen, immunological characterization, molecular characterization; gamma interferon: production

IT Alternate Indexing
Tuberculosis (MeSH)

ORGN . . .
Vertebrata, Chordata, Animalia; Mycobacteriaceae: Mycobacteria, Actinomycetes and Related Organisms, Eubacteria, Bacteria, Microorganisms

ORGN Organism Name
Mycobacterium bovis (Mycobacteriaceae): pathogen; Mycobacterium ***tuberculosis*** (Mycobacteriaceae): pathogen; human (Hominidae): patient

ORGN Organism Superterms
Animals; Bacteria; Chordates; Eubacteria; Humans; Mammals; Microorganisms; Primates; Vertebrates

L10 ANSWER 7 OF 11 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 5

AN 2000:104643 BIOSIS

DN PREV200000104643

TI Comparative evaluation of low-molecular-mass proteins from Mycobacterium ***tuberculosis*** identifies members of the ESAT-6 family as immunodominant T-cell antigens.

AU Skjot, Rikke Louise Vinther; Oettinger, Thomas; Rosenkrands, Ida; Ravn, Pernille; Brock, Inger; Jacobsen, Susanne; Andersen, Peter (1)

CS (1) Department of TB Immunology, Statens Serum Institut, Artillerivej 5, DK-2300, Copenhagen S Denmark

SO Infection and Immunity, (Jan., 2000) Vol. 68, No. 1, pp. 214-220. ISSN: 0019-9567.

DT Article

LA English

SL English

AB Culture filtrate from Mycobacterium ***tuberculosis*** contains protective antigens of relevance for the generation of a new antituberculosis vaccine. We have identified two previously uncharacterized M. ***tuberculosis*** proteins (TB7.3 and TB10.4) from the highly active low-mass fraction of culture filtrate. The molecules were characterized, mapped in a two-dimensional electrophoresis reference map of short-term culture filtrate, and compared with another recently identified low-mass protein, ***CFP10*** (F. X. Berthet, P. B. Rasmussen, I. Rosenkrands, P. Andersen, and B. Gicquel. Microbiology 144:3195-3203, 1998), and the well-described ESAT-6 antigen. Genetic analyses demonstrated that TB10.4 as well as ***CFP10*** belongs to

the ESAT-6 family of low-mass proteins, whereas TB7.3 is a low-molecular-mass protein outside this family. The proteins were expressed in Escherichia coli, and their immunogenicity was tested in cultures of peripheral blood mononuclear cells from human ***tuberculosis*** (TB) patients, Mycobacterium bovis BCG-vaccinated donors, and nonvaccinated donors. The two ESAT-6 family members, TB10.4 and ***CFP10*** , were very strongly recognized and induced gamma interferon release at the same level (***CFP10***) as or at an even higher level (TB10.4) than ESAT-6. The non-ESAT-6 family member, TB7.3, for comparison, was recognized at a much lower level. ***CFP10*** was found to distinguish TB patients from BCG-vaccinated donors and is, together with ESAT-6, an interesting candidate for the diagnosis of TB. The striking immunodominance of antigens within the ESAT-6 family is discussed, and hypotheses are presented to explain this targeting of the immune response during TB infection.

TI Comparative evaluation of low-molecular-mass proteins from Mycobacterium ***tuberculosis*** identifies members of the ESAT-6 family as immunodominant T-cell antigens.

AB Culture filtrate from Mycobacterium ***tuberculosis*** contains protective antigens of relevance for the generation of a new antituberculosis vaccine. We have identified two previously uncharacterized M. ***tuberculosis*** proteins (TB7.3 and TB10.4) from the highly active low-mass fraction of culture filtrate. The molecules were characterized, mapped in a two-dimensional electrophoresis reference map of short-term culture filtrate, and compared with another recently identified low-mass protein, ***CFP10*** (F. X. Berthet, P. B. Rasmussen, I. Rosenkrands, P. Andersen, and B. Gicquel. Microbiology 144:3195-3203, 1998), and the well-described ESAT-6 antigen. Genetic analyses demonstrated that TB10.4 as well as ***CFP10*** belongs to the ESAT-6 family of low-mass proteins, whereas TB7.3 is a low-molecular-mass protein outside this family. The proteins were expressed in Escherichia coli, and their immunogenicity was tested in cultures of peripheral blood mononuclear cells from human ***tuberculosis*** (TB) patients, Mycobacterium bovis BCG-vaccinated donors, and nonvaccinated donors. The two ESAT-6 family members, TB10.4 and ***CFP10*** , were very strongly recognized and induced gamma interferon release at the same level (***CFP10***) as or at an even higher level (TB10.4) than ESAT-6. The non-ESAT-6 family member, TB7.3, for comparison, was recognized at a much lower level. ***CFP10*** was found to distinguish TB patients from BCG-vaccinated donors and is, together with ESAT-6, an interesting candidate for the diagnosis. . .

IT . . .
Coordination and Homeostasis); Infection

IT Parts, Structures, & Systems of Organisms
T cells: blood and lymphatics, immune system

IT Diseases
tuberculosis : bacterial disease

IT Chemicals & Biochemicals
ESAT-6; T cell antigens; antituberculosis vaccine: vaccine; low-molecular mass proteins

IT Alternate Indexing
Tuberculosis (MeSH)

ORGN Super Taxa
Mycobacteriaceae: Mycobacteria, Actinomycetes and Related Organisms, Eubacteria, Bacteria, Microorganisms

ORGN Organism Name
Mycobacterium ***tuberculosis*** (Mycobacteriaceae): pathogen
ORGN Organism Superterms
Bacteria; Eubacteria; Microorganisms

L10 ANSWER 8 OF 11 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 6
AN 2000:157810 BIOSIS
DN PREV200000157810
TI Diagnosis of ***tuberculosis*** based on the two specific antigens ESAT-6 and ***CFP10*** .
AU van Pinxteren, Laurens A. H.; Ravn, Pernille; Agger, Else Marie; Pollock, John; Andersen, Peter (1)
CS (1) Department of TB-Immunology, Statens Serum Institut, Artillerivej 5, 2300, Copenhagen S Denmark
SO Clinical and Diagnostic Laboratory Immunology., (March, 2000) Vol. 7, No. 2, pp. 155-160.
ISSN: 1071-412X.
DT Article
LA English
SL English
AB Tests based on tuberculin purified protein derivative (PPD) cannot distinguish between ***tuberculosis*** infection, Mycobacterium bovis BCG vaccination, or exposure to environmental mycobacteria. The present study investigated the diagnostic potential of two Mycobacterium ***tuberculosis*** -specific antigens (ESAT-6 and ***CFP10***) in experimental animals as well as during natural infection in humans and cattle. Both antigens were frequently recognized in vivo and in vitro based on the induction of delayed-type hypersensitivity responses and the ability to induce gamma interferon production by lymphocytes, respectively. The combination of ESAT-6 and ***CFP10*** was found to be highly sensitive and specific for both in vivo and in vitro diagnosis. In humans, the combination had a high sensitivity (73%) and a much higher specificity (93%) than PPD (7%).
TI Diagnosis of ***tuberculosis*** based on the two specific antigens ESAT-6 and ***CFP10*** .
AB Tests based on tuberculin purified protein derivative (PPD) cannot distinguish between ***tuberculosis*** infection, Mycobacterium bovis BCG vaccination, or exposure to environmental mycobacteria. The present study investigated the diagnostic potential of two Mycobacterium ***tuberculosis*** -specific antigens (ESAT-6 and ***CFP10***) in experimental animals as well as during natural infection in humans and cattle. Both antigens were frequently recognized in vivo. . . of delayed-type hypersensitivity responses and the ability to induce gamma interferon production by lymphocytes, respectively. The combination of ESAT-6 and ***CFP10*** was found to be highly sensitive and specific for both in vivo and in vitro diagnosis. In humans, the combination. . .
IT . . .
Immunology (Human Medicine, Medical Sciences)
IT Parts, Structures, & Systems of Organisms
lymphocytes: blood and lymphatics, immune system
IT Diseases
tuberculosis : bacterial disease
IT Chemicals & Biochemicals
CFP-10: Mycobacterium bovis-specific antigen, diagnostic - drug;
ESAT-6: Mycobacterium bovis-specific antigen, diagnostic - drug;

tuberculin purified protein derivative
IT Alternate Indexing
Tuberculosis (MeSH)

L10 ANSWER 9 OF 11 CAPLUS COPYRIGHT 2001 ACS
AN 1999:77692 CAPLUS
DN 130:165432
TI The antigenic protein ***LHP*** of Mycobacterium ***tuberculosis*** and the ***lhp*** gene encoding it and their diagnostic and prophylactic uses
IN Gicquel, Brigitte; Berthet, Francois-Xavier; Andersen, Peter; Rasmussen, Peter Birk
PA Institut Pasteur, Fr.; Statens Serum Institut
SO PCT Int. Appl., 88 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9904005	A1	19990128	WO 1998-IB1091	19980716
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9881238	A1	19990210	AU 1998-81238	19980716
EP 1003870	A1	20000531	EP 1998-930967	19980716
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

PRAI US 1997-52631 P 19970716
WO 1998-IB1091 W 19980716
AB The Mycobacterium ***tuberculosis*** gene encoding the antigenic protein ***LHP*** that is homologous to the L45 antigen of M. bovis, is cloned and characterized. The gene can be expressed from its own promoter in slow-growing (M. ***tuberculosis*** group) and fast-growing (M. smegmatis) mycobacteria. The ***LHP*** gene product, and antigenic peptides derived from it, can be manufd. for use in vaccines and to raise reagent antibodies for diagnostic use. The promoter of the ***lhp*** gene may be of use in the expression of foreign genes in Mycobacteria. Oligonucleotides derived from the promoter region may be useful as probes or primers in the detection of M. ***tuberculosis*** in a biol. sample. Anal. of the promoters driving expression of the closely linked ***lhp*** and orf1C genes of M. ***tuberculosis*** established that they form an operon. Use of the promoter to drive expression of a reporter gene in M. smegmatis is demonstrated. The protein is abundant in short-term (7 day) culture filtrates of M. ***tuberculosis*** .
RE.CNT 9
RE
(1) Ajinomoto Kk; EP 0400973 A 1990 CAPLUS
(3) Corixa Corp; WO 9709428 A 1997 CAPLUS

(4) Corixa Corp; WO 9709429 A 1997 CAPLUS
(5) Corixa Corp; WO 9816645 A 1998 CAPLUS
(6) Corixa Corp; WO 9816646 A 1998 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT
TI The antigenic protein ***LHP*** of Mycobacterium ***tuberculosis*** and the ***lhp*** gene encoding it and their diagnostic and prophylactic uses
AB The Mycobacterium ***tuberculosis*** gene encoding the antigenic protein ***LHP*** that is homologous to the L45 antigen of M. bovis, is cloned and characterized. The gene can be expressed from its own promoter in slow-growing (M. ***tuberculosis*** group) and fast-growing (M. smegmatis) mycobacteria. The ***LHP*** gene product, and antigenic peptides derived from it, can be manufd. for use in vaccines and to raise reagent antibodies for diagnostic use. The promoter of the ***lhp*** gene may be of use in the expression of foreign genes in Mycobacteria. Oligonucleotides derived from the promoter region may be useful as probes or primers in the detection of M. ***tuberculosis*** in a biol. sample. Anal. of the promoters driving expression of the closely linked ***lhp*** and orf1C genes of M. ***tuberculosis*** established that they form an operon. Use of the promoter to drive expression of a reporter gene in M. smegmatis is demonstrated. The protein is abundant in short-term (7 day) culture filtrates of M. ***tuberculosis*** .
ST ***lhp*** gene Mycobacterium antigen cloning diagnosis vaccine; ***tuberculosis*** diagnosis vaccine antigen antibody
IT Proteins (specific proteins and subclasses)
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ESAT-6, as antigen in ***tuberculosis*** vaccines; antigenic protein ***LHP*** of Mycobacterium ***tuberculosis*** and ***lhp*** gene encoding it and their diagnostic and prophylactic uses)
IT Proteins (specific proteins and subclasses)
RL: BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(***LHP*** ; antigenic protein ***LHP*** of Mycobacterium ***tuberculosis*** and ***lhp*** gene encoding it and their diagnostic and prophylactic uses)
IT Mycobacterium ***tuberculosis***
(antigenic protein ***LHP*** of Mycobacterium ***tuberculosis*** and ***lhp*** gene encoding it and their diagnostic and prophylactic uses)
IT Escherichia coli
Mycobacterium BCG
Pseudomonas
Salmonella
(expression host; antigenic protein ***LHP*** of Mycobacterium ***tuberculosis*** and ***lhp*** gene encoding it and their diagnostic and prophylactic uses)
IT Immunoassay
Nucleic acid hybridization
PCR (polymerase chain reaction)
Test kits
(for diagnostic detection of Mycobacterium ***tuberculosis*** ; antigenic protein ***LHP*** of Mycobacterium ***tuberculosis*** and ***lhp*** gene encoding it and their diagnostic and

prophylactic uses)

IT Primers (nucleic acid)
Probes (nucleic acid)
RL: ARG (Analytical reagent use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(for diagnostic detection of Mycobacterium ***tuberculosis*** ; antigenic protein ***LHP*** of Mycobacterium ***tuberculosis*** and ***lhp*** gene encoding it and their diagnostic and prophylactic uses)

IT Mycobacterium smegmatis
(***lhp*** gene promoter functional in; antigenic protein ***LHP*** of Mycobacterium ***tuberculosis*** and ***lhp*** gene encoding it and their diagnostic and prophylactic uses)

IT Promoter (genetic element)
RL: BPR (Biological process); BUU (Biological use, unclassified); BIOL (Biological study); PROC (Process); USES (Uses)
(***lhp*** gene, expression of foreign genes in Mycobacteria using; antigenic protein ***LHP*** of Mycobacterium ***tuberculosis*** and ***lhp*** gene encoding it and their diagnostic and prophylactic uses)

IT Operons
(***lhp*** /orf1C, of Mycobacterium; antigenic protein ***LHP*** of Mycobacterium ***tuberculosis*** and ***lhp*** gene encoding it and their diagnostic and prophylactic uses)

IT Genes (microbial)
RL: BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(***lhp*** ; antigenic protein ***LHP*** of Mycobacterium ***tuberculosis*** and ***lhp*** gene encoding it and their diagnostic and prophylactic uses)

IT Protein sequences
(of ***LHP*** gene product of Mycobacterium; antigenic protein ***LHP*** of Mycobacterium ***tuberculosis*** and ***lhp*** gene encoding it and their diagnostic and prophylactic uses)

IT DNA sequences
(of ***lhp*** gene of Mycobacterium; antigenic protein ***LHP*** of Mycobacterium ***tuberculosis*** and ***lhp*** gene encoding it and their diagnostic and prophylactic uses)

IT Transcription initiation site (genetic element)
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(of ***lhp*** gene, mapping of; antigenic protein ***LHP*** of Mycobacterium ***tuberculosis*** and ***lhp*** gene encoding it and their diagnostic and prophylactic uses)

IT Physical mapping (genetic)
(of transcription initiation site of ***lhp*** gene; antigenic protein ***LHP*** of Mycobacterium ***tuberculosis*** and ***lhp*** gene encoding it and their diagnostic and prophylactic uses)

IT Plasmid vectors
(pIPX1, ***lhp*** gene of Mycobacterium ***tuberculosis*** on; antigenic protein ***LHP*** of Mycobacterium ***tuberculosis*** and ***lhp*** gene encoding it and their diagnostic and prophylactic uses)

IT Plasmid vectors

(pIPX30, expression vector for Mycobacterium using ***lhp*** promoter; antigenic protein ***LHP*** of Mycobacterium ***tuberculosis*** and ***lhp*** gene encoding it and their diagnostic and prophylactic uses)

IT Plasmid vectors
(pIPX61, ***lhp*** gene of Mycobacterium ***tuberculosis*** on; antigenic protein ***LHP*** of Mycobacterium ***tuberculosis*** and ***lhp*** gene encoding it and their diagnostic and prophylactic uses)

IT Antibodies
Monoclonal antibodies
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(to ***LHP*** gene product of Mycobacterium; antigenic protein ***LHP*** of Mycobacterium ***tuberculosis*** and ***lhp*** gene encoding it and their diagnostic and prophylactic uses)

IT Vaccines
(***tuberculosis*** , ***LHP*** protein as antigen for; antigenic protein ***LHP*** of Mycobacterium ***tuberculosis*** and ***lhp*** gene encoding it and their diagnostic and prophylactic uses)

IT 220134-86-1 220134-87-2 220134-88-3 220134-89-4 220134-90-7 220134-91-8 220325-84-8 220325-86-0
RL: BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(amino acid sequence, as antigen; antigenic protein ***LHP*** of Mycobacterium ***tuberculosis*** and ***lhp*** gene encoding it and their diagnostic and prophylactic uses)

IT 220275-47-8
RL: BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(amino acid sequence; antigenic protein ***LHP*** of Mycobacterium ***tuberculosis*** and ***lhp*** gene encoding it and their diagnostic and prophylactic uses)

IT 220275-43-4 220275-44-5 220275-45-6 220275-46-7
RL: BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(nucleotide sequence; antigenic protein ***LHP*** of Mycobacterium ***tuberculosis*** and ***lhp*** gene encoding it and their diagnostic and prophylactic uses)

IT 220163-72-4 220163-73-5 220163-74-6
RL: ARG (Analytical reagent use); PRP (Properties); ANST (Analytical study); USES (Uses)
(primer or probe for detection of Mycobacterium ***tuberculosis*** ; antigenic protein ***LHP*** of Mycobacterium ***tuberculosis*** and ***lhp*** gene encoding it and their diagnostic and prophylactic uses)

L10 ANSWER 10 OF 11 BIOSIS COPYRIGHT 2001 BIOSIS
AN 2000:139578 BIOSIS
DN PREV200000139578
TI TB diagnosis based on two specific antigens ESAT-6 and ***CFP10*** .
AU van Pinxteren, Laurens A. H. (1); Ravn, Pernille (1); Pollock, John; Andersen, Peter (1)
CS (1) Department of TB-Immunology, Statens Serum Institute, Artillerivej 5,

2300, Copenhagen S Denmark
SO Immunology., (Dec., 1999) Vol. 98, No. suppl. 1, pp. 40.
Meeting Info.: Joint Congress of the British Society for Immunology and the British Society for Allergy & Clinical Immunology. Harrogate, England, UK November 30-December 03, 1999 British Society for Allergy & Clinical Immunology
. ISSN: 0019-2805.
DT Conference
LA English
SL English
TI TB diagnosis based on two specific antigens ESAT-6 and ***CFP10*** .
IT Major Concepts
Infection
IT Diseases
tuberculosis : bacterial disease
IT Chemicals & Biochemicals
CFP10 : antigen; ESAT-6: antigen
IT Alternate Indexing
Tuberculosis (MeSH)
ORGN . . .
Animalia; Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia; Mycobacteriaceae: Mycobacteria, Actinomycetes and Related Organisms, Eubacteria, Bacteria, Microorganisms
ORGN Organism Name
M. ***tuberculosis*** [Mycobacterium ***tuberculosis***] (Mycobacteriaceae): pathogen; animal (Animalia): host; cattle (Bovidae): host; human (Hominidae): host
ORGN Organism Superterms
Animals; Artiodactyls; Bacteria; Chordates; Eubacteria; Humans;. . .

L10 ANSWER 11 OF 11 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 7
AN 1999:28278 BIOSIS
DN PREV199900028278
TI A Mycobacterium ***tuberculosis*** operon encoding ESAT-6 and a novel low-molecular-mass culture filtrate protein (CFP-10.
AU Berthet, Fancois-Xavier (1); Rasmusse, Peter Birk; Rosenkrands, Ida; Andersen, Peter; Gicquel, Brigitte
CS (1) Unite Geneitque Mycobacteriene, Inst. Pasteur, 25 rue Dr Roux, 75724 Paris Cedex 15 France
SO Microbiology (Reading), (Nov., 1998) Vol. 144, No. 11, pp. 3195-3203. ISSN: 1350-0872.
DT Article
LA English
AB The early secreted antigenic target 6 kDa protein (ESAT-6) is a potent T-cell protein antigen synthesized by Mycobacterium ***tuberculosis*** . Its corresponding gene (esat-6) is located in RD1, a 10 kb DNA region deleted in the attenuated ***tuberculosis*** vaccine strain Mycobacterium bovis BCG. The promoter region of M. ***tuberculosis*** esat-6 was cloned and characterized. A new gene, designated ***lhp*** and cotranscribed with esat-6, was identified. Moreover, computer searches in the M. ***tuberculosis*** genome identified 13 genes related to the ***lhp*** /esat-6 operon, defining a novel gene family. The transcription initiation sites of the ***lhp*** /esat-6 operon were mapped using M. ***tuberculosis*** RNA. The corresponding promoter signals were not recognized in Mycobacterium smegmatis, in which transcription of

lhp /esat-6 is initiated at different locations. The M. ***tuberculosis*** ***lhp*** gene product was identified as CFP-10, a low-molecular-mass protein found in the short-term culture filtrate. These results show that the genes encoding CFP-10 and ESAT-6 are transcribed together in M. ***tuberculosis*** and that both code for small exported proteins.

TI A Mycobacterium ***tuberculosis*** operon encoding ESAT-6 and a novel low-molecular-mass culture filtrate protein (CFP-10.

AB The early secreted antigenic target 6 kDa protein (ESAT-6) is a potent T-cell protein antigen synthesized by Mycobacterium ***tuberculosis*** . Its corresponding gene (esat-6) is located in RD1, a 10 kb DNA region deleted in the attenuated ***tuberculosis*** vaccine strain Mycobacterium bovis BCG. The promoter region of M. ***tuberculosis*** esat-6 was cloned and characterized. A new gene, designated ***lhp*** and cotranscribed with esat-6, was identified. Moreover, computer searches in the M. ***tuberculosis*** genome identified 13 genes related to the ***lhp*** /esat-6 operon, defining a novel gene family. The transcription initiation sites of the ***lhp*** /esat-6 operon were mapped using M. ***tuberculosis*** RNA. The corresponding promoter signals were not recognized in Mycobacterium smegmatis, in which transcription of ***lhp*** /esat-6 is initiated at different locations. The M. ***tuberculosis*** ***lhp*** gene product was identified as CFP-10, a low-molecular-mass protein found in the short-term culture filtrate. These results show that the genes encoding CFP-10 and ESAT-6 are transcribed together in M. ***tuberculosis*** and that both code for small exported proteins.

IT Major Concepts
Bacteriology; Infection; Molecular Genetics (Biochemistry and Molecular Biophysics)

IT Diseases
tuberculosis : bacterial disease

IT Chemicals & Biochemicals
early secreted antigenic target 6 kDA protein [ESAT-6]: T-cell protein antigen; CFP-10 protein: identification, low-molecular-mass culture filtrate protein; Mycobacterium ***tuberculosis*** esat-6 gene [early secreted antigenic target 6 kDa protein gene] (Mycobacteriaceae): characterization, transcription, promoter region, operon, cloning; Mycobacterium ***tuberculosis*** ***lhp*** gene (Mycobacteriaceae): identification, operon, transcription

IT Alternate Indexing
Tuberculosis (MeSH)

ORGN . . .
Actinomycetes and Related Organisms, Eubacteria, Bacteria, Microorganisms

ORGN Organism Name
Mycobacterium bovis (Mycobacteriaceae): strain-BCG, vaccine strain; Mycobacterium smegmatis (Mycobacteriaceae); Mycobacterium ***tuberculosis*** (Mycobacteriaceae): pathogen

ORGN Organism Superterms
Bacteria; Eubacteria; Microorganisms